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Development, evaluation and implementation of a new tool, the Efficacy Safety Score (ESS).

Doctoral thesis

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SAMMENDRAG

Adekvat smertebehandling hos opererte pasienter er viktig for en god rekonvalesens. Hovedproblemet i smertebehandling er å balansere nytte mot risiko og bivirkninger. På sengepost blir vurdering og dokumentasjon av postoperative smerter ofte usystematisk og ufullstendig, noe om kan føre til utilfredsstillende smertelindring og hindre optimale pasientforløp.

Målet med denne avhandlingen var å utvikle et nytt skåringsverktøy til støtte i rutinemessig behandling av postoperativ smerte på sengepost, med opprettholdt sikkerhet. Et slikt skåringsverktøy bør kartlegge smerte i flere dimensjoner, samt bivirkninger som kvalme/oppkast og ubehag, våkenhetsgrad, og hjerte- og lungefunksjon. Dette for å kunne identifisere pasienter som trenger ytterligere vurdering og spesifikk behandling. Skåringsverktøyet bør inkludere en anbefalt terskelverdi for å tilkalle hjelp.

Avhandlingen består av tre artikler. Den første artikkelen beskriver utviklingen og valideringen av skåringsverktøyet. Data fra en studie av 182 pasienter og et internasjonalt ekspertpanel ble brukt for å finne relevant innhold til skåren. Resultatet ble kalt Efficacy Safety Score (ESS). Vi testet deretter ESS i en studie av 207 pasienter opp mot varslingsverktøyet Modified Early Warning Score (MEWS) og informasjon fra pasientjournalene. ESS identifiserte flere hendelser angående kvaliteten på pasientbehandlingen enn hva MEWS og journalinformasjon gjorde. ESS samsvarte med MEWS og journalene om pasientsikkerhet og alvorlige hendelser.

Den andre artikkelen beskriver en studie av 195 pasienter, tilfeldig delt i to grupper for å vurdere forløpet av det første døgnet etter kirurgiske inngrep. Pasientene i den ene gruppen fikk vanlig oppfølging, mens de i den andre fikk oppfølging med ESS kombinert med trådløs måling av blodtrykk, puls, pust, oksygenmetning og temperatur (Wireless Patient Monitoring - WPM). Pasientene som ble fulgt opp med ESS og WPM ble raskere mobilisert etter operasjonen, fikk mer smertestillende, anga lavere smertenivå og høyere tilfredshet med behandlingen enn de som fikk vanlig oppfølging.

Artikkel tre beskriver en internasjonal studie ved to sykehus for å vurdere om bruk av ESS som tilkallingsalgoritme etter operasjon ville påvirke mobilisering, ikke-kirurgiske komplikasjoner og lengde på sykehusopphold. Vi fordelte 1152 pasienter tilfeldig til tre grupper; oppfølging med ESS, oppfølging med en verbal smerteskår eller til en kontrollgruppe. Vi fant ingen forskjell i grad av mobilisering eller ikke-kirurgiske komplikasjoner mellom gruppene. Gruppen fulgt opp med ESS hadde kortere sykehusopphold enn kontrollgruppen.

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SUMMARY

Adequate treatment of postoperative pain and minimising side effects is essential for optimal patient recovery. The main problem in pain treatment is balancing benefits against risk and side effects. Unfortunately, for postoperative patients on the hospital ward, monitoring, assessment and documentation of quality issues, like pain and nausea, are often non-systematic and inadequate, leading to insufficient pain relief.

This thesis aimed to develop a new score as a supportive tool for routine postoperative pain management while maintaining patient safety. The score should assess key recovery quality parameters such as multidimensional pain, nausea/vomiting and discomfort, and basic safety parameters like level of consciousness and respiratory and circulatory function. The goal should be to identify patients needing further specific diagnostics and treatment. The score should hence include a call-out algorithm to get assistance when required. Three published papers support this thesis.

Paper I describes the development of the new Efficacy Safety Score (ESS) using data from a pilot study of 182 patients followed by a consensus process to identify relevant score items. We tested the ESS in a prospective observational study of 207 patients against Modified Early Warning Score (MEWS) and routine journal data. The ESS identified more issues regarding the quality of care than MEWS and journal information. The ESS correlated with MEWS and journal information on safety issues and serious adverse events.

Paper II describes a randomised controlled study of 195 patients receiving standard care or intervention with the ESS combined with continuous wireless patient monitoring (WPM) of vital signs. The aim was to investigate if the ESS and WPM systems would improve clinical outcomes. The intervention resulted in more rapid mobilisation, more dedicated use of opioids, lower pain levels and increased patient satisfaction.

Paper III describes an international prospective observational study at two hospitals. We assessed the influence of ESS' call-out algorithm on postoperative pain management and its side effects on length of hospital stay (LOS), mobilisation and non-surgical complications. We randomly assigned 1152 patients to three groups; follow-up with ESS, follow-up with a verbal pain score or a control group. We found no difference in the degree of mobilisation or non-surgical complications between the groups. However, the group followed up with ESS had a shorter LOS than the control group.

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My mother Kari died too early to experience my education and this work. I believe she would have been proud of my achievements. To my father Torodd for all support.

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Stadsbygd, July 2022

CONTENT

LIST OF PAPERS

Paper I: Skraastad E, Ræder J, Dahl V, Bjertnæs LJ, Kuklin V. Development and validation of the Efficacy Safety Score (ESS), a novel tool for postoperative patient management. BMC Anesthesiol. 2017;17(1):50. Published 2017 Mar 28. doi:10.1186/s12871-017-0344-0

Paper II: Skraastad EJ, Borchgrevink PC, Nilsen TIL, Raeder J. Postoperative quality and safety using Efficacy Safety Score (ESS) and a wireless patient monitoring system at the ward: A randomised controlled study. Acta Anaesthesiol Scand. 2020;64(3):301-308. doi:10.1111/aas.13492

Paper III: Lisa Dybvik, Erlend Skraastad, Aigerim Yeltayeva, Aidos Konkayev, Tatiana Musaeva, Igor Zabolotskikh, Lars Bjertnaes, Vegard Dahl, Johan Raeder, Vladimir Kuklin, "Influence of a New “Call-Out Algorithm” for Management of Postoperative Pain and Its Side Effects on Length of Stay in Hospital: A Two-Centre Prospective Randomized Trial", Pain Research and Management, vol. 2017, Article ID 9431984. https://doi.org/10.1155/2017/9431984

ACRONYMS

ASA	American Society of Anesthesia
APS	Acute Pain Service
CI	Confidence interval
CPOX	Continuous pulse oximetry
ECG	Electrocardiogram
ERAS	Enhanced Recovery After Surgery
ESS	Efficacy Safety Score
HR	Heart rate
IOM	Institute of Medicine
LOS	Length of hospital stay
MEWS	Modified Early Warning Score
MCID	Minimum clinically important differences
NEWS	National Early Warning Score
NSAID	Nonsteroidal anti-inflammatory drug
OIRD	Opioid-induced respiratory depression
OMEQ	Oral morphine equivalent
OR	Operating room
ORADE	Opioid-related adverse drug event
OSAS	Obstructive sleep apnoea syndrome
PACU	Post-anaesthesia care unit
PCA	Patient controlled analgesia
PONV	Postoperative nausea and vomiting
POSPOM	Preoperative Score to Predict Postoperative Mortality
POSSUM	Physiologic and Operative Severity Score for the enUmeration of Mortality and morbidity
PPSP	Persistent postsurgical pain
PROM	Patient-reported outcome measures
VNRS	Verbal numeric rating scale
VR	Ventilatory rate
WPM	Wireless patient monitoring

1. INTRODUCTION TO THESIS

"For the secret of the care of the patient is in caring for the patient."

Francis W. Peabody, MD, Oct 1925

1.1 Topic

This thesis examines the effects on quality of care and patient safety early after surgery using a novel clinical decision score, the Efficacy Safety Score (ESS), to manage postoperative pain and its side effects on the ward. The processes of development, validation and implementation of the new score in a Norwegian and international setting from 2014 to 2019 are described and evaluated.

1.2 Perspective

Acute postoperative pain is common and remains underestimated and undertreated, although recognized as a major postoperative quality issue for decades.[1-4] Opioid analgesics are still the mainstay of postsurgical pain treatment and introduce a challenging balance between adequate pain control against harmful side effects.[5,6] In 2009, Norwegian media reported a tragic incident: a 22-year-old man with severe acute postoperative pain died on a surgical ward from an overdose of pain medication the night after knee surgery.[7] More reports followed with the same message: patients were at risk of potentially catastrophic consequences after surgery when admitted to spare-staffed wards.[8,9] For me, this was an eye-opener. In addition, as head of a surgical department then, I knew that some nurses started crying when starting night shifts, given the singlehanded responsibility of up to ten newly operated patients on the ward. If just one of these patients needed some extra attention due to inadequate pain relief or other reasons, that would jeopardise the regular follow-up of all the others.

The nurses often only reported information about the patient's condition at the end of the shift every eight hours, then in a combination of written and oral transfer to the proceeding shift. The first versions of early warning scores, such as MEWS,[10] were introduced at the hospital, but they were short in important quality aspects , e.g. pain assessment and postoperative nausea and vomiting (PONV) for patients after surgery. To ensure a better

quality of care and patient safety and improve the employees' working conditions, these apparent weaknesses in our health care systems should be addressed and corrected.

I discussed this with my good colleague Dr Vladimir Kuklin. Our hospitals lacked a systematic and simple way to evaluate the numerous postoperative ward patients. We believed finding more objective measurements than complex subjective descriptions of the patient's status, mixed with varying clinical experience among an overworked ward staff, should be possible. We hypothesised that patients and health care professionals responsible for postoperative care and pain treatment on the ward may benefit from the feedback of a straightforward but still comprehensive score for safe pain management. The score should survey real-time status and changes over time. Status should include patients' postoperative perceived quality, including analgesia at rest and when mobilising, as well as minimal side effects. Safety aspects of sedation, and respiratory and circulatory parameters should be registered. Finally, the score should include a call-out algorithm for the staff to get physical help and/or medical guidance.

I hope with this thesis to draw attention to the early postoperative phase on the ward where the nurses often are left alone handling a group of patients in a challenging clinical setting. Furthermore, by bringing forward a new evaluation system and a simplified score, I hope to contribute to improving the quality of postoperative pain management.

1.3 Review of research

Surgery is an essential part of modern health care, and it is estimated that 313 million operations are performed annually worldwide.[11] In Norway, there are approximately 385 000 surgical operations each year, of which 51% are for inpatients.[12]

When subjecting a patient to surgery, there will be some harm induced by the surgical intervention, but this should be for the benefit of significant health improvement as a final result of the same procedure. Also, the harm should be minimised regarding temporary quality and safety problems.

The characteristics of the surgical procedure and the underlying disease and/or condition have traditionally determined the care of patients going through major surgery. Even with indisputable variances in patient-related and procedure-related risks, most surgical patients

go through one pathway of care. They share standard facilities for preoperative assessment, anaesthesia, operating rooms, post anaesthesia care units (PACUs), and hospital wards.[13]

The interaction between the impact of surgery, anaesthesia and inflammatory response with the individual patient's physiological condition, reserves and psychosocial life situation is important[14]. The type and quality of surgery are modulators in this interaction;[15] however, they are not the only players. Adopting this latter perspective, the individual assessment and treatment of each patient's needs and postoperative pain relief are mandatory.

1.3.1 Acute postoperative pain

"*Pain is whatever the experiencing person says it is, existing whenever he says it does*."
Mary Margo McCaffery, RN, 1968

Among healthcare professionals' core responsibilities are the prevention and alleviation of pain. Failure to treat pain is viewed worldwide as poor medicine, unethical practice, and a violation of a fundamental human right.[16,17] In addition, fear of postoperative pain is a prominent patient concern before surgery and may lead to high anxiety levels preoperatively.[1,4] However, despite increased attention and knowledge, significant postoperative pain is still frequent.[2,18]

The International Association for the Study of Pain (IASP) defines *pain* as ''an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage".[19] The aetiology of acute postoperative pain is multifactorial. Surgical interventions result in tissue and nerve fibres damage and initiate multiple responses in the neuromatrix,[20] from sensitisation of peripheral and central pain pathways to feelings of anxiety, fear and frustration.[21] Biological, psychological, and social factors influence differences in the pain experience.[22-24]

Pain is a personalised, conscious experience crucial for survival.[25] However, the acute pain associated with surgery is unwanted and generally not purposeful.[3] If postoperative pain is not well managed, early mobilisation, oral nutrition and recovery will be delayed and incapacitate the patient from joining rehabilitation programs.[26,27] This may lead to inferior outcomes. Postoperatively, suboptimal pain management may contribute to medical complications, such as deep vein thrombosis, pneumonia, infection, chronic pain and

depression.[28] Pain is also one of the most common medical causes of delayed discharge after ambulatory surgery[29]. Despite the numerous guidelines on managing acute pain introduced over the past two decades,[30-33] surveys suggest that there has been little improvement for many patients during this period.[2,18] In a study of postoperative pain in 14 Norwegian hospitals, 38 % of the patients reported a mean pain intensity ≥4 and 11 % a mean ≥6 on an 11-point scale.[34] These numbers are equal to those from a cross-sectional observational study of more than 15000 patients in the UK,[35] where 11 % reported severe pain and 37% reported moderate pain during the first 24 postoperative hours.

Acute postoperative pain should normally resolve during the healing process within two to three months.[36] The definition of persistent postoperative pain (PPSP) is pain developed after a surgical procedure of at least 3–6 months' duration.[37] The intensity and length of acute postoperative pain are associated with the transition to PPSP.[38-40] However, a definite cause-relationship has been hard to establish.

1.3.2 Postoperative pain treatment

Inadequate management of postoperative pain, whether undertreatment or overtreatment, have negative consequences for patients: including increased length of hospital stay or readmission, impaired rehabilitation, increased risk of persistent postoperative pain, and adverse events related to excessive analgesic use, such as oversedation.[41] A combination of different drugs and methods, so-called multimodal analgesia, is used to balance efficacy, side effects and risks.[42,43] Non-opioids, opioids and adjuvant drugs are available as part of pharmaceutical pain therapy, and the use of specific opioid-sparing techniques, including regional analgesia, is encouraged to improve patient outcomes.[44,45] The introduction of new analgesic drugs is slow, and few new drugs have come into the market in the last decades. The main innovations have been in better understanding and implementation of older drugs, new delivery systems and routes of administration.[46]

The basis for postoperative pain alleviation is still paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), a single-dose glucocorticoid, local anaesthetics and opioids as needed.[6,47] Generally, analgesic medications act by inhibiting ascending pain signals in the periphery or centrally in the spinal cord and brain. Some also facilitate descending inhibitory pathways of the spinal cord. These mechanisms lead to decreased nociceptive transmission

and interpretation of these signals as pain by higher neurological centres.[18] Multimodal analgesia involves choosing a medication that acts on different parts of the anatomical pain pathways. Drugs with different mechanisms of action are combined to produce additive or synergistic effects, allowing the use of lower doses, thus reducing side effects from single-drug strategies. In acute postoperative pain therapy, a ladder regimen is recommended[6]: Step 1 - Basic postoperative pain management: paracetamol, NSAIDs, a glucocorticoid and infiltration with local anaesthesia into the wound. Step 2 - If necessary, supplement with one or more of the following: epidural pain management, peripheral nerve block, opioid via a patient-controlled pump, peroral opioid and/or catheter-based local anaesthetic infiltration. Step 3 – Consider extra drugs for patients or procedures with a risk of severe pain or any contraindications for the basic medication: preoperative gabapentinoids, single-dose clonidine administration at the end of the surgery, and/or intravenous ketamine and lidocaine infusion during surgery and at the PACU. A short-acting opioid should be prescribed as needed on top of all steps.[48] In recent years, the sequence of steps 2 and 3 have been modified in many guidelines. Some step 3 measures may be used before considering regional anaesthesia or extended opioids.[49]

Non-pharmacological techniques

Due to concerns over the side effects of traditional pharmacotherapies, non-pharmacological interventions to aid postoperative pain management are becoming increasingly investigated. These interventions are often cheap and easy to implement and can be used throughout the perioperative phase. Strategies include patient education and psychological interventions, e.g. cognitive-behavioural therapy[50] and distraction techniques, e.g. music.[51]

Side effects from opioid pain treatment

Opioids have long been the cornerstone treatment for moderate and severe acute pain.[18] However, there is a balance of pain relief benefits in postoperative pain treatment versus the risk of harmful side effects. Opioids have many dose-related side effects ranging from bothersome to life-threatening, including itching, nausea, vomiting, fatigue, urinary retention, constipation, somnolence, hypotension and respiratory depression.[52] In the immediate postoperative phase, these opioid-related adverse events (ORADEs) occur

commonly. In one surgical cohort, 11% of all the patients reported ORADEs, and it was related to worse patient outcomes.[53]

In addition to sedating effects, opioids cause ventilatory impairment by acting directly on respiratory centra and indirectly by depressing the laryngeal muscular tonus.[54-56] Opioid-induced ventilatory impairment is a type-2 respiratory failure associated with opioid administration and high arterial pressure of CO_2 with or without hypoxemia.[57] Included in the respiratory physiological changes induced with acute opioid use are the depression of the hypercapnic ventilatory response and hypoxic ventilatory response.[56] This may impose a risk of undetected hypoventilation if supplemental oxygen overrides the hypoxic ventilatory drive and only pulse oximetry is being relied on for patients at risk of opioid-induced respiratory depression (OIRD).[56] OIRD is a significant cause of death and brain damage for postoperative patients and is a feared complication in postoperative treatment.[58] A challenge is that the definition of OIRD varies in the literature, from the narrow spectre of naloxone utilization to the broader assessment of bradypnea and hypoxemia.[54,59]

Fatal overdoses from postoperative pain medication are rare, but this is still a major safety issue.[60] The first 24 postoperative hours comprise the highest risk period, according to published reports on adverse respiratory depression events associated with opioid administration.[61] In a 20 years retrospective study on 357 closed malpractice claims associated with OIRD, most of the events (88%) occurred within 24 hours of surgery.[60] Furthermore, 97% of these events resulting in death or permanent brain damage were classified as preventable with better monitoring and response, and only 25% of these patients with fatal OIRD had obstructive sleep apnea syndrome (OSAS) as a known risk in advance. Obstructive sleep apnoea syndrome (OSAS) and opioid-induced ventilatory impairment are frequently associated, with this interrelationship being complex and often unpredictable.[62]

Due to the diversity in methods of pain relief and clinical settings, as well as the complex and unpredictable physiological responses of each patient, a multidimensional approach to evaluating the postoperative patient is called upon to maintain patient safety.[63,64] An international multidisciplinary consensus statement from 2021 on the prevention of postoperative opioid-related harm lists up these recommendations to best clinical practice for the postoperative period in hospital:

- do not use unidimensional pain scores alone but also functional outcomes to guide the provision of opioids,
- try to identify abnormal pain trajectory early, use multimodal analgesia,
- use titrated doses of immediate-release opioids only,
- do not use long-acting opioids and compound opioid analgesic formulations, and
- evolve hospital strategies for mitigation of opioid-induced ventilatory impairment, specified by assessing the level of sedation at appropriate and repeated intervals.[57]

1.3.3 Status of postoperative treatment

The postoperative period starts when ending surgery, and the patient is transferred from the operation room (OR) and lasts until the patient has fully regained the expected final level of function. The goal of postoperative care is to promote healing, prevent complications and steadily return the patient to optimal health.[65,66] The classical postoperative pathway implies transferal from the OR to the PACU and then to the ward before subsequent discharge to home. However, there are alternative pathways in ambulatory surgery where patients are discharged directly home from PACU or can bypass the PACU. Also, after major surgery and/or fragile or unstable health situation, patients may be sent from the OR to the intensive care unit or another high-facility care unit rather than the PACU.

1.3.4 The PACU

During the immediate postoperative period, the patient needs to safely regain consciousness, receive appropriate postoperative care with pain control, re-establish normal physiologic functions and have their vital signs monitored closely. This is most often done at a specialised department (PACU) for recovery with monitoring capacities and sufficient staffing, following given standards.[67]

How long the patient stays at the PACU depends on the type and length of surgery, type of anaesthesia, the status of eventual regional anaesthesia, the patient's general pathophysiology and preoperative health. Ideally, all patients should be in a PACU-like environment as long as there is any risk of vital organ failure after a surgical procedure. However, this will imply an extensive use of resources, and in most cases, for no benefit. Hence, there must be a cutoff when the condition is regarded as safe for the patient to be transferred to the ward. However, such a cutoff always implies a small but calculated risk of

severe events happening on the ward. Therefore, determining readiness for discharge is often according to a checklist or a score, e.g. a version of the Aldrete score.[68-70] Fulfilling this, postoperative patients should, upon ward arrival, be: fully awake, having no or little pain or nausea, able to move voluntarily, have a regular and adequate respiratory frequency, maintain acceptable oxygen saturation in room air, maintain stable blood pressure and have a heart rate within acceptable limits, partly based on pre-anaesthetic levels.

1.3.5 The ward

This thesis focuses on pain management and its side effects on the ward after surgery. Most patients will recover to a status of stable physiology after the first hours postoperatively in the PACU and continue to improve function during their hospital stay. Nevertheless, some patients do not follow this desired path of postoperative development and need extra attention and care. Even being clinically fit with fulfilled discharge criteria for discharge from PACU, the condition may change later. This may be a problem for the ward, especially with increasing pain or discomfort due to analgesic medication wearing off or any physiological deterioration after initial safe arrival. Identifying and having time to take care of these individual cases can be difficult in busy everyday work on the wards, where the logistic system is designed for streamlined patient pathways of improved condition with time. While the patient is in the PACU with continuous monitoring and observation by sophisticated monitoring and highly trained staff, there are abundant tools and measures available to ensure both quality of the treatment and safety. However, fewer health care professionals and monitoring resources are available after discharge to an ordinary ward. Furthermore, the lack of systematic and objective approaches to managing postoperative patients are often a reality on the ward.[71]

Limited resources

An association between larger nurse staffing levels on the ward and better outcomes in surgical patients has been shown.[72] Also, recruitment and resources need to be directed at training and retaining high-quality, specialised nurses for surgical wards and improving nurse-patient ratios.[73]

The EuSOS cohort study from 2012 on postoperative mortality including 46 539 patients, revealed that 1574 (3.4%) patients died on the ward after surgery. This constituted 84% of all the in-hospital deaths in this study.[13]

Still, the ward is a logical step toward recovering to a habitual situation for the patients with less stressful surroundings. It is also easier to maintain normal social interaction with other people on the ward and to have visitors. Getting back to regular daily routines such as eating and drinking, toilet visits, showering, and mobilisation is essential for all patients. The idea of patients drinking, eating and mobilising (DrEaMing) at 24 hours postoperatively is used as a marker of functional recovery.[18,74]

1.3.6 Special systems and algorithms for postoperative ward care

Multiple scoring systems and scores are available for assessing the patients in the postoperative period on the ward. For example, there are scores for long-term outcomes and surgical recovery,[75,76] cognitive recovery and resumption of capacities,[77,78] and scores for acute medical deterioration.[10,79] Also, there are risk scores for postoperative delirium,[80] predictions of respiratory complications,[81] and risk of postoperative nausea and vomiting.[82] However, these are most typically designed for a specific purpose and not for a comprehensive longitudinal evaluation of patient status and evaluation of quality and safety issues in combination. Furthermore, many of these scores are extensive and cumbersome to perform, hence not suitable for frequent audits for each postoperative patient.

Acute Pain Service (APS)

A formalised APS with a multimodal and multidisciplinary approach is recognized as an important tool in improving postoperative pain management on surgical wards.[83] Apart from optimising the multimodal use of analgesic drugs, the APS may include more advanced techniques, such as intravenous opioid patient-controlled analgesia (PCA), epidural analgesia and other regional techniques.

Enhanced Recovery After Surgery (ERAS)

Implementations of the ERAS protocols improve short-term outcomes and reduce hospital stay length.[84,85] The goal of ERAS is the optimal use of resources and clinical interventions to reach equitable and efficient care, and strict fulfilment of the protocols is most beneficial.[86]

However, reductions in length of hospital stay and logistics concerning the enhanced recovery pathway are of limited value to the patients if no concomitant patient-reported outcome measure (PROM) improvement exists.[87]

1.3.7 Perioperative mortality

"*Death during surgery is now rare, but postoperative death is not.*"

P.J. Devereaux, NEJM, 2015

The number of deaths within 30 days after surgery is estimated to be at least 4.2 million annually worldwide, and half of these postoperative deaths occur in low- and middle-income countries.[88] These postoperative deaths account for 7.7% of all deaths worldwide[89] and make postoperative death the third most common cause of death after ischemic heart disease and stroke.[88]

However, perioperative mortality has declined significantly over the past five decades despite increasing patient baseline risk.[90] The International Surgical Outcomes Study (ISOS) in 2014, a global prospective study in 27 countries of elective inpatient surgery, revealed a mortality rate of 0.5%.[91] Still, the earlier mentioned large European cohort study (EuSOS) of patients admitted for elective, urgent, and emergency non-cardiac inpatient surgery revealed a 4% in-hospital mortality.[13] For the Norwegian hospitals enrolled, 1,5% of the patients died during the hospital period. The diversity in the different national numbers indicates possible potential for significant improvement. Even a low rate of avoidable harm will be associated with many preventable deaths because of the high numbers of surgical procedures performed.

After non-complicated surgery and anaesthesia, unexpected severe postoperative patient safety problems are rare. The anaesthesia-related mortality rate (anaesthesia as the primary or contributing cause) is reported at approximately 1:100 000 – 1:150 000, though with wide variations due to methodological differences.[92] The anaesthesia-related mortality risk is related to patient age and preoperative physical status. The American Society of Anesthesiologists (ASA) physical status classification system is widely used worldwide to classify a patient's physical fitness before surgery, ranging from I-V where I is a normal healthy patient.[93] In a large French patient material, the anaesthesia-related hospital mortality in the total material was 1:18 500. For ASA classification I patients, the risk was

1:250,000, in ASA classification II patients 1:20 000, for ASA classification III patients 1:3700 and for ASA classification IV patients 1:1 800.[94] The association of increased risk with higher ASA classification is strong, but the ASA score does not consider the type of surgery. Furthermore, it is based on subjective criteria and not properly adjusted for age. Other validated scores, e.g. the Preoperative Score to Predict Postoperative Mortality (POSPOM) and the Physiologic and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM), have better accuracy and reliability in predicting postoperative mortality.[95,96] In the United Kingdom, approximately 10% of the patients are at high risk of getting postoperative complications, and these patients count for 80% of postoperative deaths.[97,98]

1.3.8 Postoperative monitoring – safety

> "It may seem a strange principle to enunciate as the very first requirement in a Hospital that it should do the sick no harm." Florence Nightingale, Notes on Hospitals, 1863.

The WHOs definition of *patient safety* is "the prevention of errors and adverse effects to patients associated with health care." The U.S. Institute Of Medicine proclaims this definition of patient safety:[99] "Freedom from accidental injury; ensuring patient safety involves establishing of operational systems and processes that minimise the likelihood of errors and maximise the likelihood of intercepting them when they occur."

Postoperative patients are at risk of clinical deterioration, which must be minimised using monitoring, assessment and observation skills in postoperative care[100]. With the increasing age and complexity of comorbidity in postsurgical patients, the proper monitoring of the vital signs, i.e. heart rate, respiration rate, oxygenation, blood pressure and body temperature, is important.[101]

For safety issues, i.e. identification of medical deterioration, so-called early warning scores are widely used.[79] The development of these scores is for standardising surveillance of vital functions. However, usually, they are intermittent, user-dependent, do not include patient quality parameters and are often based on cumbersome manual registration.[79] For instance, acute cardiorespiratory deterioration is often preceded by an 8- to 12-hour period of subtle changes in vital signs.[102,103] Therefore, changes in cardiorespiratory physiology are often

missed or detected too late to prevent patients from progressive and severe medical deterioration.

Postoperative hypoxemia and respiratory depression

Hypoxemia is common in the immediate postoperative phase due to incomplete lung re-expansion, pain and surgical injury causing reduced diaphragmatic and chest wall activity, impaired hemodynamics and residual effect of anaesthesia (most important eventual residual neuromuscular blockade), which may cause atelectasis, ventilation-perfusion mismatch, alveolar hypoventilation and impaired upper airway patency.[104,105] This is mainly a concern for the PACU period but may also affect the patient after discharge to the ward.

A study from Cleveland in 2015 reported that hypoxemia (defined as the saturation of peripheral oxygen measured using pulse oximetry [SpO_2] of <90%) was common and prolonged in 594 out of 833 included patients during their first 48 hours on a surgical ward after non-cardiac surgery. Blinded continuous pulse-oximeter recordings showed that the nurses missed 90% of the hypoxemic episodes in which saturation was <90% for at least one hour.[106] Transient postoperative ventilatory insufficiencies and hypoxemia are common after non-cardiac surgery in patients receiving opioid analgesia on the general ward.[106,107]

Intermittent measuring of SpO_2 may not detect ward hypoxemia reliably because the hypoxemic episodes might occur between the sparse assessments of vital signs.[108]

While continuous pulse oximetry is mandatory in the PACU, there has not been a tradition of using this device on the Norwegian wards, except in situations of clear clinical deterioration or known hypoxia. This may have to do with a large number of false alarms and artefacts with a pulse-oximeter in the ward situation, with many movements and mobilisation of the patients. Also, even for continuous pulse oximetry (CPOX), the evidence of impact on clinically relevant outcomes like reduced ICU transfer and mortality is inconclusive.[109] In a systematic review, CPOX at the ward was superior at detecting hypoxemia but did not per se reduce the complications or risk of dying after anaesthesia.[110]

Hypoventilation is a state of decreased or inadequate ventilation: breathing is too shallow or too slow to meet the body's needs, resulting in hypercarbia and hypoxemia.[111] This is also called respiratory depression.

As pulse oximetry monitors oxygenation,[112] it has reduced sensitivity as a monitor of hypoventilation if supplemental oxygen is administered. Thus, as a single measure, without other observation or monitoring of ventilation, it is "not without potentially serious limitations".[113] Slow respiratory rate is regarded as a good predictor of respiratory depression, given that proper measurements are performed.[114 115] Rhythm generation is the most opioid sensitive aspect of respiration, and changes in the respiratory pattern are commonly seen in patients receiving opioids and observed at lower opioid doses than those needed for a decline in tidal volume.[116] Still, significant postoperative hypercapnia may also evolve in the presence of normal RR and SpO_2 in patients receiving opioids due to non-ability to maintain a free airway,[117] which warrants the use of continuous capnography/capnometry for high-risk patients.[113] Capnography is shown superior to routine respiratory counting and pulse oximetry in identifying postoperative respiratory depression,[107,118] when caused by the central effects of opioids.[54]

Cardiac complications

Almost half of all in-hospital cardiorespiratory arrests occur on the wards, with significantly worse outcomes than similar events in monitored environments.[119-121] Cardiac complications (i.e., sudden cardiac death, myocardial infarction, acute heart failure, and cardiac arrhythmias) account for at least one-third of all perioperative deaths in non-cardiac surgery.[122] The remaining main causes of perioperative deaths are consequences of stroke, septicemia, and haemorrhage, which often result in an unplanned critical care unit (ICU) admissions.[123,124]

Postoperative hypotension

Hypotension is common during the immediate postoperative period and is often unrecognized or may persist for a prolonged duration due to intermittent assessments of vital signs on the ward.[108 125] From the POISE-II (PeriOperative Ischemic Evaluation-2) cohort, and other reports, there is emerging evidence that prolonged hypotension is strongly and consistently associated with myocardial injury, acute kidney injury, delirium, stroke and death and can usually be controlled.[125-128] Thus, a 2019 consensus statement on postoperative blood pressure for elective surgery concludes that a systolic pressure <90 mm Hg or <30% below baseline is likely to put most patients at risk of end-organ injury and that a greater frequency of postoperative blood pressure measurement is likely to identify the risk

of harm and clinical deterioration earlier.[129] That said, in a study from 2021 on 68 000 patients, postoperative hypotension without intraoperative hypotension was not associated with major adverse cardiac or cerebrovascular events, and there was no interaction between post- and intraoperative hypotension for any of the outcomes investigated.[130]

Still, a stable and adequate blood-pressure is a pre-requisite for a patient to be discharged from the PACU to the ward.

1.3.9 Quality of health care

"Quality is never an accident; it is always the result of high intention, sincere effort, intelligent direction and skilful execution; it represents the wise choice of many alternatives." *John Ruskin*

One way of looking at quality in health care is to which extent expectations are met. However, one may argue that expectations in many patients may be too low and thus not an optimal source for reference. Harteloh gives a more abstract definition: "Quality [is] an optimal balance between possibilities realised and a framework of norms and values."[131] This latter definition reflects that quality is an abstraction and does not exist as a discrete variable. The Norwegian Directorate of Health says high-quality healthcare:[132]

- is effective
- is safe and secure
- involves users and gives them influence
- is coordinated and characterised by continuity
- make good use of resources; and
- is available and fairly distributed

Others have tried to define health care quality in terms of standards. The U.S. Institute of Medicine defined *quality* as "the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge."[133] This led to a definition of quality as listings of quality indicators, as expressions of the standards. Most listings of quality indicators are composed of the negative 5Ds: Death, disease, disability, discomfort, and dissatisfaction.[134] Others have proposed expanding these, using positive components of quality indicators, such as regaining the status of health, achievement of appropriate self-care, health-related quality

of life, perception of being well cared for, and symptom management.[135] Many view "Quality Health Care" as the overbuilding in which patient safety is the keystone. An example is the Institute of Medicine which claims patient safety to be "indistinguishable from the delivery of quality health care".[99]

In sum, thorough postoperative care is crucial to ensuring positive outcomes for patients after surgery. The foci of postoperative care should be re-establishing the patient's physiological balance, pain management and prevention of complications to help the patient recover to health.

There is a need to improve the quality of postoperative treatment in terms of better analgesic therapy and reduction of side effects with maintained patient safety. Furthermore, there is a need to monitoring a patient's general status and efficacy and side effects of the treatment given as a routine audit over time. Lastly, there is a need for a to-the-point and correctly addressed communication about concerns and problems for postoperative patients on the ward.

2. AIMS OF THE THESIS

The overall aim of this thesis was to develop a new score as a supportive tool for routine multidimensional management of postoperative pain and its side effects, with maintained safety, for patients on the surgical ward.

We broke this down into specific aims related to the quality of care and patient safety in this setting. These specific aims were:

1. To identify clinical useful outcome variables of major importance for the postoperative ward patients' status, regarding the quality of care and safety.
2. To extract and condense the complex clinical situation of a postoperative ward patient into simple assessments and summarise these into a new clinical score for management of postoperative pain and its side effects to be validated for routine use.
3. To see if the new score could influence established patient outcome variables.
4. To investigate if the safety and patient-perceived quality of postoperative treatment could be potentially improved, using the new score on the ward combined with new technology for monitoring the patient physiology.

3. MATERIALS AND METHODS

"There is no such thing as a perfect method. Methods always can be improved upon."

Walter Daiber

3.1 Study design and descriptions

Study 1 part A used a modified Delphi-process[136] with three iterations until it was reached consensus on the score's contents. We predefined consensus as more than 80% agreement between the participants. After revision, the score was called the Efficacy Safety Score (ESS).

The Delphi method is an iterative process that uses a systematic progression of repeated rounds of voting and is effective for reaching expert group consensus where there is little or no definitive evidence, and opinion is important.[137] In its original version, the Delphi method was used quantitatively to forecast events, but later, its use was expanded to make decisions.[138] However, the characteristics of the method are still preserved in the modified version: anonymity, iteration and feedback. The anonymity of the process minimises domination by individuals in the expert group and reduces group pressures for conformity.[136] The multistage approach is the essence of the Delphi method, with each stage building on the previous results.

We conducted study 1 part B as a prospective observational study to monitor postoperative inpatient status with the ESS during the first postoperative 24 hours to validate the ESS score.

Study 2 was a single centre randomised controlled trial (RCT) with two parallel groups; a standard care group and an intervention group using the ESS combined with wireless patient monitoring (WPM) for the first 24 postoperative hours on a surgical ward. The study's design and description adhered to the Consolidated Standards of Reporting Clinical Trials statement (CONSORT),[139] and the study was formally monitored by the Faculty of Medicine and Health Sciences, NTNU, according to Norwegian Clinical Research Infrastructures Networks (NorCRINs) procedure of good clinical practice (GCP). We developed the study protocol with the help of a patient representative to ensure user involvement. After obtaining patients' written informed consent preoperatively for study enrolment, the patients were randomly assigned to one of two groups using a random number generator and sequentially

numbered opaque sealed envelopes a priori.[140] Neither the staff nor patients could be blinded to group allocation.

Study 3 was a two-centre prospective randomised observational study with three groups; an ESS group, a group with an assessment of pain using the verbal numeric rate scale (VNRS group), and a control group. After inclusion, we randomly assigned the patients to one of the three groups using sealed envelopes.

3.2 Participants

In study 1, part A, we used an international panel of ten experienced anesthesiologists.

In study 1, part B, the inclusion criteria were all elective patients expected to be treated and observed at least for one hospital overnight stay after surgery. Exclusion criteria were patients <18 years of age or with poor communication capabilities. We enrolled 207 patients.

For study 2, we chose one surgical unit as the investigation site, identified eligible patients from the operating theatre lists of mixed surgery and recruited participants during preadmission or when prepared for surgery. Inclusion criteria were patients undergoing acute or elective surgery expected to be hospitalised on the surgical ward for more than 24 hours postoperatively. Exclusion criteria were patients <18 years of age, poor communication capabilities or when planned surgery was incompatible with mobilisation during the first 24 hours. We consecutively asked 201 patients to participate, and 200 were included and randomly assigned to two groups.

For study 3, we considered all surgical patients expected to need observation in the hospital for more than 8 hours. Exclusion criteria were patients <18 years of age, patients with poor communication capabilities and patients who refused to communicate. We evaluated 1200 patients for inclusion; 48 patients did not meet inclusion criteria, giving 1152 patients to be included and randomly assigned to three groups.

3.3 Measurement, data collection and outcomes

3.3.1 Study 1 A and B

Initially, we searched the literature and found several postoperative assessment scores.[68-70,75-78,141,142] However, since we found no simple system constructed for comprehensive monitoring of the general status and efficacy and side effects of pain treatment after discharge from PACU, we developed a prototype score tool. In study 1, part A, an international expert group of ten specialists in anaesthesia made suggestions about the information needed to adequately evaluate the state of the clinical condition after discharge from PACU.

In study 1, part B, we collected clinical data to validate the score against published general criteria, "The Quality for Health Status Questionnaires criteria", for verbal scores set out by Terwee et al.[143] We also validated the ESS in a group of patients encompassing independent scoring by two nurses and compared the ESS with the modified Aldrete score[68] and the Modified Early Warning Score (MEWS),[10] which focus on safety aspects of recovery. This pilot study suggested that an ESS ≥10 was an appropriate cut-off value for severe problems needing immediate consultation with a physician. For this reason, we prospectively tested the cut-off value of ≥10, allowing for a post hoc evaluation of the proper cut-off value. As this study was performed with an explorative hypothesis-generating intent, we performed no formal power calculation.

We performed study 1, part B at the Departments of Anaesthesiology, High dependency Unit, General Surgery, Orthopaedics, Obstetrics and Gynaecology, and Ear-, Nose- and Throat at Kongsberg Hospital, Kongsberg, Norway.

In study 1, part B, the nursing staff registered ESS on paper sheets hourly for the first 8 hours postoperatively and then every 4 hours for the next 16 hours on the ward.

In parallel, we collected information on several parameters from the complete journal of the patient: pain, nausea and vomiting, and medication given during the first 24 postoperative hours. Further registrations were time to readiness for discharge from PACU, not-scheduled contacts/visits by a physician, re-admittance to high dependence unit or re-operation, results of MEWS on the ward, time spent at recovery unit, total hospital stay and 30-days mortality.

3.3.2 Study 2

Intervention group

In this group, the nurses assessed the ESS in parallel with electronic automatic retrieved vital signs from the WPM, which monitored: heart rate, ECG, ventilatory frequency, axillar skin temperature, blood pressure (initiated manually each time the nurses assessed the ESS) and finger pulse oximetry from wireless and wearable sensors. The WPM also provides the National Early Warning Score (NEWS). The other registrations for the ESS (i.e., pain, nausea, side effects and mental state) were collected by questioning and noted on a portable tablet. In addition, we extracted information on the given medication from the patients' charts.

Standard care group

In the standard care group, NEWS was performed on paper formularies at least every 12 hours or with increased frequency in the presence of increased symptom severity. In addition, the frequency of postoperative pain evaluation and notes about pain assessment and management were registered together with given medication extracted from the patients' charts.

Ordinary postoperative protocol

Both groups followed the same protocols and indications for medication set up by the hospital's guidelines.

We conducted study 2 at the Orkdal Dept., St. Olavs Hospital, Trondheim University Hospital, Norway.

Outcomes: The primary outcome of study 2 was time to full mobilisation, defined as being able to walk more than one step with/without support.

Secondary outcomes were average postoperative pain for the first 24 hours, milligrams of postoperative administered opioids (OMEQ) during the same period, overall patient satisfaction on a 5-point scale, number of documented NEWS and pain assessments, presence of postoperative nausea and retching/vomiting, unscheduled postoperative interventions, postoperative complications and length of hospital stay (LOS).

All patients completed a questionnaire 24 hours postoperatively (Appendix A), including questions about mobilisation, average pain, postoperative nausea and retching/vomiting, sleep, anxiety, self-reported safety and security, mental function and satisfaction. We also registered unscheduled physician visits due to postoperative clinical issues, supplementary oxygen, and re-admissions to the PACU or intensive care unit.

3.3.3 Study 3

In study 3, we collected clinical data to investigate if control of postoperative pain treatment and its side effects by using ESS might influence the degree of mobility and morbidity in surgical patients and consequently reduce LOS.

We performed the study in the departments of abdominal surgery, orthopaedics, gynaecology, urology, and vascular surgery and high dependency units at Astana University Hospital, Astana, Kazakhstan, and Krasnodar University Hospital, Krasnodar, Russia.

Outcomes: The study's primary outcome was to assess LOS in groups of patients with different types of clinical data records and "call-out algorithms". Secondary endpoints were to compare the degree of mobilisation, the number of postoperative non-surgical complications, and 28-day survival between the groups.

In all groups, we recorded the mobility degree hourly for the first 8 hours postoperatively. In addition, we registered and sampled all subjective and objective clinical data at each hospital in an especially designed program for iPad® and subsequently transferred these to the Structured Query Language (SQL) database.

In the ESS group, a "call-out" decision for ESS ≥ 10 was established for consultation by telephone or visit by the responsible anesthesiologist or acute pain team on duty. In the VNRS group, we based the "call-out" decision on VNRS > 4 at rest, while in the Control group, a "call-out" decision was based on the judgement of the patient's clinical condition by a nurse.

Nurses in surgical departments and high dependency units recorded all clinical variables and mobility degree, while research fellows collected all demographic variables. The latter also registered all postoperative non-surgical complications, such as cardiovascular and

pulmonary symptoms during the first 8 hours after surgery, and contacted all patients or their relatives by telephone to verify 28-day survival.

3.4 Statistical methods

In study 1, we conducted the statistical analyses using one-way analysis of variance (ANOVA), estimating intra-class correlation coefficient (ICC) and post hoc Bonferroni correction. For between-group differences when comparing the data by sex and ASA-score, we used repeated-measures ANOVA.

In study 2, we used Kaplan-Meier estimators to analyse group differences in time to mobilisation and performed a log-rank test to compare time to event distributions. Additionally, we used Cox regression to estimate hazard ratios for time to mobilisation between the intervention and control group, adjusting for age, ASA classification and sex. Finally, we used linear regression to estimate mean differences between the groups for opioid medication doses, numbers of pain assessments and NEWS performed, and pain intensity adjusting for age, ASA classification and sex. A 95% confidence interval gives the precision of estimated effects. Categorical variables, such as reported oxygen therapy, postoperative nausea and retching/vomiting, were analysed using Chi-square tests. Due to few expected categorical variables in some groups, we used Fischer's exact test to analyse patient satisfaction.

In study 3, we performed statistical data analyses with cluster analyses of an intracluster correlation coefficient, one-way ANOVA, and Chi-square analysis. Data distribution was assessed using the Shapiro-Wilk test, and we used the Kruskal-Wallis one-way analysis of variance on ranks to compare the difference between groups. If F value was greater than the critical value, ANOVA was followed by Dunn's method for pairwise multiple comparisons to obtain P values between groups. Additionally, we retested the "null hypothesis" by removing patients with extreme values of LOS from the data analysis, defining patients with LOS below the 5th percentile and above the 95th percentile of the median as outliers and removing them from the LOS data of each hospital, the clustered LOS data of both hospitals, and the LOS data of all patients after laparoscopic cholecystectomy.

3.5 Ethical considerations and approvals

The Regional Committee for Medical and Health Research Ethics South-East judged Study 1 to be a quality assessment exempt from the patient's informed consent (ref 2014/580 A). Furthermore, the Local Data Inspectorate of Vestre Viken Hospital Trust, Drammen, Norway (ref 2015/4793) approved the patient protocol.

Study 2 was approved by the Regional Committee for Medical and Health Research Ethics (reference number 2017/1903/REK South East A) and registered at clinicaltrials.gov (NCT03438578).

Ethical approval of study 3 was provided by the Ethical Committee of Scientific Research Institute of Traumatology and Orthopaedics, Astana, Kazakhstan (ref. 2014-002), and the Ethical Committee of Kuban State Medical University, Krasnodar, Russia (ref. 2014-027). In both countries, the project was considered a quality assessment exempt from the patient's informed consent.

3.6 Financial support

During the studies in this thesis, no study participant, co-authors or co-workers received any financial benefits or payment. The principal investigator (Erlend Johan Skraastad) received financial support and sponsorship from The Norwegian Medical Association's foundation for quality improvement and patient safety and The Norwegian Society of Anaesthesiology to develop the ESS. In 2018, the principal investigator received a two-year scholarship from The Joint Research Committee between St. Olavs hospital and the Faculty of Medicine and Health Sciences, NTNU (FFU). For study 2, Isansys Lifecare Ltd. (U.K.) lent us the monitoring hardware and provided free or reduced pricing supplies without any conditions to influence the study design or reporting.

4. RESULTS - SUMMARY OF PAPERS

"However beautiful the strategy, you should occasionally look at the results"
Ian Gilmore

We present the results from each of the three papers contributing to this thesis.

4.1 Paper I

"Development and validation of the Efficacy Safety Score (ESS), a novel tool for postoperative patient management."

The aim of paper I was to develop and formally validate the ESS.

We used the three-round consensus process result to revise the prototype score on the issues of consciousness and general condition into the ESS used in the subsequent validation study. See Appendix B for the first-round response from the expert panel.

The ESS consists of five clinical features regarding the patient's postoperative status: mental condition, postoperative nausea and vomiting (PONV), pain at rest, pain at movement and general condition. Depending on the patient's status or complaints, each clinical feature is scored from 0 to 15 and summarised in a total score (Figure 4-1).

We suggest an ESS ≥10 as an appropriate cut-off value for problems in need of someone staying with the patient and immediate consultation with a physician. A call-out value of ESS ≥10 correlated with MEWS > 0 values and journal information about postoperative concerns with a sensitivity of 94% and 92%, respectively. A value of ESS≥10 identified all serious safety issues.

A subgroup analysis showed differences over time and between age groups and type of surgery in mean ESS for the 24-hours observation period. With the ESS, we identified a higher number of patients experiencing quality and safety issues than routine care and MEWS: 121 patients had an ESS≥10 while 103 patients had a note in their journal about a postoperative concern and/or a MEWS>0. In addition, we obtained positive ratings for six out of seven tested criteria of questionnaire quality; one criterion had an indeterminate rating.

Conclusions: ESS fulfils the suggested criteria for score quality validation and adequately reflects the patient's postoperative status with high sensitivity.

Paper I contributes to the first aim of this thesis and fully covers the second aim.

Figure 4-1. The Efficacy Safety Score.

Efficacy Safety Score (ESS)		
Status	Description	Points
1. Mental status	Awake and alert patient	0
	Awake patient, but influenced by drugs. Difficulties in communication.	5
	Acutely confused, upset/uneasy, hallucinated or euphoric patient	10
	Unresponsive patient	15*
2. Postoperative nausea and vomiting (PONV) status	No postoperative nausea or vomiting	0
	Postoperative nausea only	5
	Postoperative nausea and vomiting/retching	10
3. Pain status at rest	No postoperative pain	0
	Low intensity postoperative pain (VNRS 1–3)	1-3
	Moderate intensity postoperative pain (VNRS 4–6)	4-6
	Severe intensity postoperative pain (VNRS 7–10)	7-10
4. Pain status during movement	No postoperative pain	0
	Low intensity postoperative pain (VNRS 1–3)	1-3
	Moderate intensity postoperative pain (VNRS 4–6)	4-6
	Severe intensity postoperative pain (VNRS 7–10)	7-10
5. General condition status	No remarks	0
	Minor discomfort (e.g. light-headedness, minor itching, blurred vision, decreased urination etc.)	5
	Excessive discomfort (e.g. severe dizziness, itching, restlessness, urine retention, sensation of cold/warmth, cold sweating)	10
	Acute circulatory abnormalities (blood pressure ≤80 or ≥200 mmHg, heart rate ≤40 or > 110)	15*
	Acute respiratory abnormalities (dyspnoea, respiration rate < 9 or >20/min, long pauses in breathing, shallow breathing)	15*
*Any single score of 15 (on either consciousness, circulation or respiration) should call for IMMEDIATE activation of acute assistance with the patient.		

4.2 Paper II

"Postoperative quality and safety using Efficacy Safety Score (ESS) and a wireless patient monitoring system at the ward: A randomised controlled study."

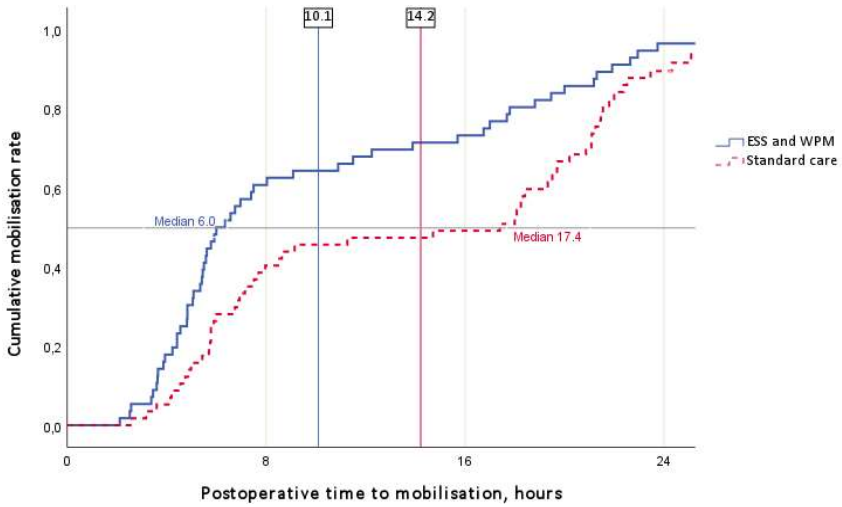
Paper II aimed to investigate if the ESS combined with a WPM system in the first 24 hours after discharge from PACU would improve clinical outcomes for patients on one general surgical ward.

Mean time to postoperative mobilisation was 10.1 hours for patients in the intervention group compared to 14.2 hours for patients in the standard care group (Figure 4-2); this corresponds to an adjusted hazard ratio of 1.54 (95% CI 1.04-2.28). The intervention group patients received a higher dose of oral morphine equivalents (OMEQ); 25.5 mg vs 15.2 mg, P<0.001; reported lower intensity of pain on a 0-10 scale; 2.1 vs 3.3, P<0.001; and had higher patient satisfaction on a 5-point scale; 4.9 vs 4.3, P<0.001. The length of hospital stay was similar between the groups; 70.9 hours in the intervention group vs 76.6 hours in the standard care group, P=0.58. No serious side effects were registered in the intervention group, whereas we registered two in the standard care group.

Conclusions: Introducing ESS combined with WPM resulted in improved pain management, increased satisfaction and more rapid mobilisation for patients in this study.

Paper II contributes to the first and third aims of this thesis and fully covers the fourth aim.

Figure 4-2. Kaplan-Meier one minus survival plot for time (hours) until postoperative mobilisation. Mean lines.



4.3 Paper III

"*Influence of a new "call-out algorithm" for management of postoperative pain and its side effects on length of stay in hospital: A two-centre prospective randomized trial."*

Paper III aimed to evaluate the influence on LOS by recording ESS hourly in the immediate postoperative phase with the application of a "call-out algorithm". We performed this study in two university hospitals where the routine policy of registration of postoperative pain at the ward had not been adopted yet.

LOS was significantly shorter with 12.7±6.3 days (mean ± SD) in the ESS group versus 14.2±6.2 days in the control group ($p<0.001$). We found no significant differences between the groups' mobility degree, the number of postoperative non-surgical complications, number of postoperative non-surgical complications, or 28-day mortality.

Conclusion: Postoperative ESS recording, combined with the possibility of calling upon an anesthesiologist when exceeding the threshold score, might have contributed to the reductions of LOS in this two-centre study.

Paper III contributes to this thesis' third specific aim.

5. DISCUSSION

"Do the best you can until you know better. Then when you know better, do better."
Maya Angelou

The main findings from the three papers supporting this thesis are that the Efficacy Safety Score (ESS) fulfils suggested criteria for score quality validation and reflects the patient's postoperative recovery status adequately and with high sensitivity. A call-out value ≥10 for calling for enforced attendance and help was found appropriate and might influence clinical outcomes like LOS. Introducing the ESS as a clinical decision tool combined with a wireless monitoring system (WPM) of patient vital signs resulted in earlier postoperative mobilisation, more dedicated use of opioids, less pain, and more satisfied patients during the ward part of the first 24 postoperative hours, compared to standard care.

5.1 Discussion of main findings

The purpose of the ESS is to give the nursing staff on the ward a simple tool for analysing the patient's postoperative recovery status, emphasising pain management. It does not include all aspects of postoperative care and is not designed to explore the degree of severity of the patient's condition in detail. Instead, it consists of specific aspects of potential recovery problems summarised to a single number as a call-out algorithm. We developed the score to identify patients who need their postoperative care adjusted in a busy daily care environment, not to surveil medical deteriorated or critically ill patients on the ward. The goal is to make a simple judgement of every patient with specific questions on clinical concerns important for the postoperative ward patient.

Validation

No empirical evidence exists concerning the final quality criteria when developing health-status questionnaires. The criteria suggested by Terwee et al.[143] are based on the Scientific Advisory Committee of the Medical Outcomes Trust,[144] and are explicit requirements for the formal validation of questionnaires. Still, the Terwee et al. checklist is not a gold standard to determine the quality of a questionnaire or determine the best questionnaire in an everyday clinical situation. However, the checklist is a recognized tool providing a systematic review of measurement properties to rate the quality of a questionnaire or test battery. It is

considered helpful when introducing a new scoring system. We addressed and fulfilled seven out of eight validation criteria suggested by Terwee et al.[143]

A novel score

A legitimate question is whether we need a new score when many scores and clinical tools are available. Nevertheless, to our knowledge, there is no other score in the literature than the ESS, which focuses on multidimensional pain management and summarises the patient's postoperative status for daily routine clinical use. Bowyer and co-workers identified 11 different scoring tools for recovery status, checking and documentation and concluded that the Postoperative Quality of Recovery Scale (PQRS) best assessed recovery in all relevant domains, including physiological, nociceptive, emotive, activities of daily living, cognition and patient satisfaction.[145] However, as the PQRS is designed with 24 items to cover the entire postoperative course, from leaving the operating room until the resumption of normal activities at home, it is perceived as cumbersome and time-consuming to use. It also needs a baseline registration of the preoperative status, has high complexity and is user-dependent. For these reasons, the authors conclude that PQRS is not suited for a busy everyday clinical practice[145]. Other scoring systems are available and extensively used, such as the early warning scores MEWS[10] and NEWS[79] and the Aldrete score.[68]

The Aldrete score is specially designed as a dichotomous "yes" or "no" tool for PACU discharge, with no grading of safety and quality issues. Furthermore, it does not consider the progression of postoperative status with time. The early warning scores are simple systems on safety issues only and do not consider other quality aspects. The latter was evident in our test of the MEWS versus ESS in study 1. Implementing early warning scores is not consistently shown to have the anticipated impact on improved clinical outcomes for patients[146-148]. For surgical ward patients specifically, studies show significant concerns for lack of concordance of early warning scores with patients' clinical status during the first postoperative 24 hours.[149,150]

Postoperative mobilisation

The intervention with ESS and WPM resulted in earlier postoperative mobilisation compared to standard care. Good quality of ward recovery could be based on the acronym DREAMS (Drinking, Eating, Analgesia, Mobilising and Sleeping) on day one after surgery.[74] This

assessment of broader postoperative abilities, rather than assessments of physiological parameters at single postoperative time-points, aligns with the ESS concept. Mobilisation is a suggested golden goal for anaesthesia outcomes because it encompasses the return of a spectre of physical capabilities.[74] The benefits of early mobilisation are shown for various postoperative patients.[151] New technology for remote and wireless patient monitoring can increase patient safety and quality without interfering with early mobilisation.[152,153]

Postoperative opioid use

The patients in the intervention group with ESS and WPM in study 2 received significantly more opioids than the controls. We found this associated with earlier mobilisation and increased patient satisfaction due to improved pain relief. The mean intensity of postoperative pain for the standard care group is similar to the result presented in a previous Norwegian study regarding postoperative pain management.[34]

However, not all ESS and WPM group patients received opioids on the ward. The nurses identified those with pain and provided these patients with efficient on-demand pain relief with maintained safety. Our interpretation is that the frequent surveillance with the ESS tool made the nurses pick out and monitor those patients with an individual higher need of opioids and treat them accordingly with better pain results and no increase in side effects. The probability of receiving extra opioids for postoperative pain relief is significantly larger if a pain score is documented.[154] The absence of pain assessment and documentation is associated with suboptimal postoperative pain management,[155] which is congruent with our findings for the standard care group in Paper II, with the total lack of documentation on pain for 17 out of 99 patients.

Advocating for aggressive pain management by increased opioid use in the early postoperative phase may be controversial from a side effect point of view and the risk of potential abuse later on. However, our patients were inpatients with expected moderate to severe postoperative pain. Most of them received a comprehensive multimodal non-opioid pain prophylaxis, i.e. paracetamol, NSAIDs, glucocorticoid and local anaesthesia wound infiltration or nerve blocks. In this setting, early intravenous titrated administration of morphine in repeated boluses is an efficient and effective way to control moderate-to-severe acute postoperative pain.[156,157] Early appropriate pain treatment, including higher

doses of opioids for a short period of a few days, maximises analgesia and reduces the risk of misuse by reducing overall consumption and length of prescription.[158] The latter is essential; as reported in 2017, about 6% of U.S. surgical opioid-naïve patients continued their postoperative opioid prescriptions three months after surgery.[159]

More opioid treatment in the ESS and WPM intervention group in study 2 did not increase postoperative ORADEs, e.g. emetic symptoms or respiratory problems. Furthermore, we did not find more drowsiness from more opioids in this group. The opposite seemed to be the situation, as these patients had earlier mobilisation and a tendency for a shorter hospital stay. These findings differ from studies where higher doses of opioids are associated with an increased risk of adverse events and increased LOS for surgical patients.[52,160] The reason for these differences might be more frequent and systematic assessment - and multidimensional evaluation - of postoperative pain using the ESS in our setting.

Patient satisfaction

Improved pain relief may explain the increased patient satisfaction in the ESS and WPM group. Still, other factors like being continuously monitored, regularity in follow-up, and interactions with health care providers are probably also important. In addition, when patients become active participants in their care, they become more comfortable and able to function.[64]

Quality of care and patient safety

Previously reported perceptions from point-of-care electronic bedside charting show a reduction in the probability of documentation errors.[161] Furthermore, continuous vital sign measurements and automated advisory monitors reduce the time required by nurses to measure vital signs, leading to a quicker response when needed.[162] The nurses in our study provided supplementary oxygen to twice as many patients in the ESS and WPM group compared to the standard care group, reflecting a beneficial effect of continuous monitoring.

While SpO_2 was used in study II, it is not a parameter of the ESS as validated and tested in study I, which may be considered an inconsistency. The circulatory - and respiratory threshold levels for ESS, when developed in 2013-2014, were based on the initial MEWS criteria. SpO_2 was not included in MEWS or used regularly at Norwegian wards at that

time.[10] Probably, for that reason, the oxygen saturation did not reach the level of consensus for inclusion in the construction of the ESS in study 1. The intended use of ESS is on the ward where access to medical equipment for such measurements was – and still is – limited.

The ESS focuses on balancing the benefits and risks of side effects in pain management. Given that opioids are commonly used postoperatively, respiratory rate (RR) and level of sedation were included in the ESS to detect OIRD.[101,115,163] In a study of machine learning methods in more than 260,000 ward patients, RR had the highest "weight" in the predictive algorithm for predicting clinical deterioration, followed by heart rate, systolic blood pressure, and SpO_2.[164] The National Institute for Health and Care Excellence In the UK, stated that "RR is the best marker of a sick patient and is the first observation that will indicate a problem or deterioration in condition" (https://www.nice.org.uk/guidance/CG50). The 2021 international consensus statement, which looked specifically on prevention of postoperative opioid-related harm, states that sedation is currently the most reliable clinical marker of postoperative opioid-induced ventilatory impairment.[57]

A Danish study of 112 patients from 2020 with continuous monitoring revealed severe nocturnal oxygen desaturation (SpO_2<85% for≥10 minutes) occurring in 35% of the patients during the first postoperative week. Interestingly, desaturation to SpO_2 < 88% also occurred in 48 patients (43%) before surgery.[165] This reflects that the normative polysomnography minimal value of SaO_2 for adults during sleep (i.e. 87% for age 50-64, and 84% for age 65-79)[166] are below the threshold set for hypoxemia as used in NEWS (e.g. < 92%). It may be suggested that a preoperative 24-hour baseline assessment should be done for each patient, but the benefit of such a measure has not been demonstrated. Furthermore, this will conflict with our intention of making a simple, feasible score for postoperative wards. However, since 2014 the development of reliable and cost-effective equipment for continuous measurements of peripheral oxygen saturation and capnometry available for ward use have been in progress. Wireless technology, not conflicting with postoperative patient mobilisation or sensitive data concerns, suggests including a threshold level for SpO_2 in a future revision of the ESS. This will be in accordance with the recent recommendations from 2021 for future hospital ward monitoring.[167]

Regarding complications noted in the intervention group in study 2, i.e. atrial fibrillation and hypotension, they had the potential of progressing more seriously but were discovered at an

early stage. Postoperative atrial fibrillation (POAF) frequently occurs after noncardiac surgery and is often unrecognized due to spontaneous conversion to sinus rhythm.[168] Prolonged and untreated POAF is associated with a higher risk of stroke, myocardial infarction, and all-cause mortality following noncardiac surgery.[169] Transient postoperative hypotension after noncardiac surgery in patients without intraoperative hypotension is not associated with major adverse cardiac or cerebrovascular events but induces a risk for acute kidney injury, readmission and increased risk of 30-/90-day mortality.[130] The three events referred to from study 2 were all asymptomatic, and all regained normal physiology spontaneously or after fluid therapy, with no further intervention needed. These cases, described in Paper II, where the ESS and WPM identified postoperative patients at risk of deterioration, is an indication of the ESS and WPM being suitable for detecting safety issues. However, the study was not powered to conclude on significant safety benefits.

Communication

In paper III, we introduced the call-out algorithm in ESS to ease access to help and guidance for postoperative patients when needed. This realises one of the main goals for developing ESS: easier communication leading to more help and guidance from the physician on call for the nursing staff. Objective measurements can make the nurses more confident in their clinical judgment, decision-making, and reporting. Also, reporting and communication between doctors and nurses may be more to-the-point when using objective signs of patient safety and well-being. The quality of patient care may improve with the standardisation implicit in automatic electronic nursing documentation.[170]

The working situation on the ward

Accurate clinical documentation is needed to coordinate and communicate patient care effectively.[171] Still, documentation occupies a substantial amount of nurses' working time, and interventions to reduce the nurses' time on clinical documentation are called upon.[172] The ESS is routinely conducted bedside in less than one minute, and combined with a WPM, it can simplify postoperative monitoring and documentation.

5.2 Methodological considerations

Making inferences about cause and effect is not always a straightforward procedure, and choosing the most appropriate study design is crucial as it affects precision and validity.

5.2.1 The Delphi method

The literature search did not give us data to make a systematic review on postoperative assessment of both patient quality and safety issues. Therefore, to answer the first aim of this thesis, we chose to use the Delphi method to identify the most crucial outcome variables for evaluating the status of the postoperative patient on the ward. The Delphi method is not superior to other ways of achieving consensus, but we found it suitable and adequate for our purpose. The method addresses "what could/should be" rather than the more common "what is",[173] and is a recommended process for developing clinical guidelines.[174] The expert panel selection is the most important step in the Delphi process because it directly relates to the quality of the results generated.[175] There are no defined criteria to guide the selection of subjects for the expert panel. Still, individuals are eligible if they have related backgrounds and experiences concerning the target issue. Further, they should be capable of giving helpful inputs and be willing to revise their initial or previous judgments to reach a consensus.[176] The modified Delphi method has been heavily criticised due to potential selection bias in the expert panel, and Goodman (1987) warns about "the pitfalls of illusory expertise" and "potentially misleading title of expert".[177] We chose participants from personal knowledge to experts who had clinical and scientific approaches to their work as consultant anesthesiologists, acknowledged academic credentials, and interest in postoperative treatment. There is no agreement on how to report from a Delphi method. However, we should have reported our criteria on expert panel selection according to recommended methodologic criteria for reporting of Delphi studies.[178] Furthermore, our expert panel of ten clinically experienced males from northern Europe is not demographically representative of our profession. The optimal number of participants in a Delphi study is not established in the literature,[136] but some suggest 10-15 participants being sufficient.[179]

Loughlin and Moore (1979) suggested that consensus should be equated with 51% agreement among the expert panel.[180] Others claim a percentage measure is inadequate, suggesting stability on repeated iterations to be a more reliable measurement.[181]

5.2.2 The validation study

To test out the effect of ESS properly, we would like to do a randomised controlled trial to establish causality. However, to do so, we first needed to validate the ESS. Validation is the act of confirming something as true or correct, with either a gold standard or a true incidence or situation in an infinite population. There is no gold standard for validating health-related questionnaires or scores, and validation is a challenging and not straightforward issue. The criteria set up by Terwee et al.[143] provide a systematic review of measurement properties to rate the quality of a score, and therefore we chose these to validate the ESS. Observational studies are not designed to explore causal effects but can describe associations between applied measures and outcomes.[182] We chose this design to develop and validate ESS as a clinical score reflecting the postoperative patients' status. This study addresses the second specific aim of this thesis.

5.2.3 The randomised controlled study

The fourth aim of this thesis was to investigate if introducing the ESS as part of a monitoring system could improve postoperative quality and safety. The randomised controlled trial is the highest scientific standard in establishing causality, useful to test the effect of a single intervention given its fundamental criteria of a properly randomised allocation.[183] The decision to include all eligible patients in one ward may have made the results more variable and statistically less favourable to our system with the ESS and WPM. As in our study, most surgical patients undergo surgery with little or no trouble during their hospital stay regarding postoperative treatment. These patients are often in a fast-track system, undergo minimally invasive surgery, have few concomitant illnesses, are treated with multimodal pain management and often receive regional anaesthesia. We could have chosen a restricted patient population of those going through surgical interventions with more needs postoperatively and higher risks of deterioration, such as total knee arthroplasty, open thoracic surgery or spinal fusion. However, this project aimed to develop a system to be functional generally on the ward, with usability for the total surgical population.

We deliberately presented the nurses with the ESS and the wireless monitoring equipment with minimal introduction and training before the study started. This is a risky study method; the staff could have jettisoned the whole project. Recommendations for successful implementation of innovations are generally to thoroughly educate, motivate and train the personnel and make support available.[184] Our strategy was that if professionals do not readily recognize and find the new tool for their well-known work tasks useful, this tool may need redesign.

We report on mean, not median times, for mobilisation in Paper II. Reporting on median times would have given a larger difference between the groups because the distribution of mobilisation times results is right-skewed, with the mean greater than the median, and the right-skewed distribution is more pronounced for the intervention group. Still, we chose to report on mean times because the area under the curve, including outliers, reflects the clinical workload for the health care professionals better.

5.2.4 The "call-out algorithm" study

To answer the third aim of this thesis, we investigated the influence of recording ESS and the application of a "call-out algorithm" in two university hospitals in which the routine policy of registration of postoperative pain on the ward had not been adopted yet. LOS is used as a proxy for hospital care.[185] The interaction between less pain and faster postoperative recovery has been documented, focusing on the clinical consequences of adequate pain management.[186] Moderate-to-severe pain at rest and reduced mobility after surgery are shown to be associated with longer LOS, and the authors suggest that improved pain control might reduce LOS.[187]

In study 3, we found no differences between the three groups in pain, the degree of mobility, number of postoperative complications or 28-day survival. Thus, we were not able to show that the reduction in LOS were associated with less pain or better mobilisation. It may be speculated that the non-blinded design of the study may have contributed to bias in terms of better motivation in both patients and personnel for a faster hospital discharge.

5.2.5 Systematic error

When looking at the association between intervention and outcome, one has to consider alternative explanations that could affect the results in observational studies. Without randomisation, all other factors are not equal and may vary systematically. Bias and confounding are two main sources of systematic errors, not affected by sample size.

Information bias is when information from participants is incorrect or missing. Other names for this are observational bias or misclassification.[188] Differential misclassification occurs when the probability of being misclassified differs across groups of study subjects, while nondifferential misclassification is when all groups or categories of a variable have the same probability of being misclassified.[189]

Selection bias refers to errors due to the selection of participants. This potential is present in selecting the expert panel in the Delphi process in study 1, given that we used subjective, personal knowledge of everyone's clinical and scientific work. In study 3, the randomisation of patients into the three groups came out biased for the University Hospital of Krasnodar results as we found significant differences between the groups regarding ASA classification, type of surgery, and anaesthesia.

5.2.6 Methodological bias

In study 2, the obvious extra monitoring equipment made it impossible to blind participants and health care professionals to group allocation. Especially looking at patient satisfaction, this could lead to a measurement bias increasing the difference between the groups. The patients, and staff, who received the intervention, may feel selected and stimulated by the group allocation per se. One large group of initially included patients (i.e. radical prostatectomy) turned out to have restrictions from the surgeon in terms of no mobilisation until the day after surgery. This led to a prolonged cluster of these patients' mobilisation time due to non-functional causes. We removed these patients from the analysis of this primary outcome.

In study 2, we rely on self-reported measures in the questionnaire, which is subject to potential biases. When using self-reporting the potential for behavioural contagion, social desirability, underreporting, and item-misinterpretation is always present. Behavioural

contagion, meaning an increased tendency to copy behaviour from socially related persons,[190] is possible on a single ward with patients having social contacts. Social desirability bias is a response bias of a tendency where the participants (i.e., in a survey) answer in a manner considered favourable by others. This may lead to overreporting "good" behaviour and underreporting unwanted behaviour.[191] However, in the same study, the alternative approach to observed objective variables were used as well, with a similar beneficial outcome in the study group.

5.2.7 Confirmation bias

Emphasising one hypothesis because it does not contradict investigator beliefs is called confirmation bias or observer bias. Using the same study personnel through study 2 and not new independent persons is a potential confirmation bias. The risk for bias when developing a questionnaire survey for a specific aim, as in study 2, is imminent. Bias is a pervasive problem in the design of questionnaires.[192]

5.2.8 Confounding

Confounding occurs when the true association between two factors is confused by one or more other factors.[188] A confounder must fill three criteria: it must be associated with the exposure; it must be a risk factor for the outcome, and it cannot be an intermediary link in the causal chain between exposure and the outcome. Confounding can be controlled for in the study design, e.g. through randomisation or later in data analysis using multivariable regression analysis. In study 2, we used Cox proportional hazards regression and adjusted for the confounding factors age, ASA-classification and sex; as these were the confounders, we a priori judged clinically relevant.

5.2.9 Random error

Opposed to systematic errors, random error is a statistical error due to chance, is unpredictable and does not recur. It causes variability in the data we cannot explain, and we can never exclude it from affecting precision to some extent. The role of chance can be estimated using statistical analysis, and random errors will decrease with increasing sample size. A confidence interval (CI) will estimate the risk of random error, given the assumption of no systematic error. A CI is constructed by the point estimate plus/minus its standard

error (SE) multiplied by a chosen confidence level, usually 1.96, to get a CI of 95%. A CI of 95% around the point estimate includes the true estimate of interest 95 out of 100 times. The sample size is a major determinant of the width of the CI, and in our setting a sample size of about 200 participants in study 2 were judged to give sufficient precision.

5.2.10 Generalisability

After evaluating if a study has internal validity, e.g. given study design, bias and confounding, we can consider the external validity or generalisability. For example, are our results applicable to other populations and hospitals? The sites for Study 1 and Study 2 in this thesis are minor hospitals and departments. The participants and patients come from Norway's homogenous and mainly Caucasian population. Furthermore, the surgery offered at the study hospitals limits the patient categories included in studies 1 and 2. The generalisability of this thesis' results should therefore be interpreted with caution. In study 2, we deliberately chose not to include only special or complex patient categories, as we wanted to see how the intervention influenced a random part of this ward's mixed everyday patient population. This gives diversity and hence more generalisable results. In study 3, we introduce a broader demographic spectre with a higher proportion of major surgery and elderly patients, and hence claim an improved generalisability for using the ESS.

5.3 Clinical implications

Postoperative patient safety

The ESS does not improve patient safety per se. Still, it gives the health care professionals a tool that, with a high degree of certainty, identifies patients at risk and helps separate them from the vast majority of postoperative patients doing well. In addition, systematic questioning with to-the-point communication improves safety. This systematic approach to patients can be made in many ways, while regularity is vital. Quality and safety go hand in hand, and patient safety is a responsibility that needs continuous attention from the health care systems. To ensure patient safety, the healthcare systems must strive to prevent errors, learn from the errors that occur, and create a culture of safety that involves healthcare professionals, organisations, and patients[193].

Quality of postoperative patient care

With the focus from hospitals on patient turnover and reducing the length of hospital stay, the patients have little time to learn to become patients. For example, we expect the patients to speak up about discomfort and pain. Also, if there is none in the room, they have to pull the cord of the nurse call system on their initiative, which is neither optimal nor safe if a sudden emergency occurs.

The structured setup, fixed questions, and a less person-dependent assessment of the ESS might be reassuring. Patients repeatedly asked the structured questions of ESS about PONV and pain both at rest and at movement might become more confident in optimal postoperative progression. They adapt to a more active, educated and satisfied patient role: they learn that movement and mobilisation are good and that adequate relief of pain and nausea is essential.

Wireless patient monitoring and bedside documentation

During the entire course of a hospital stay, the monitoring is fragmented and not coherent, involving multiple placements and replacements of monitoring devices. These include the pre-hospital setting/ambulance, the emergency room, the pre-anaesthetic room, operating theatre, PACU and eventually the ward. Each location usually has wall-mounted equipment with variable degrees of automated storage capacities. Documentation is often done on separate charts or electronic patient journal solutions. The monitoring is not continuous on the standard hospital ward; the equipment usually circulates among multiple patients, and documentation is irregular. The risk of missing valuable data and information about patients' clinical trends is imminent. We have shown in Paper II that performing the documentation process at the bedside right after assessing patient status is an advantage, both for the patients and the healthcare workers. Especially, assessment and documentation are fundamental for managing pain successfully, as acute pain is a perceived experience that needs addressing as quickly as possible.[154]

Clinical indicators of quality health care

"However, not everything that can be counted counts, and not everything that counts can be counted." William Bruce Cameron

It is thoroughly described for health care services that quality consists of multiple dimensions. Thus, when assessing the total quality of care or treatment, an effort should be made to identify these dimensions before putting them together as a whole[194]. Classification can be the structural dimensions (e.g., infrastructure and resources, expertise, available equipment, registers), the process dimension (activities in the patient course, e.g., diagnostics, surgical procedures) and the outcome dimension (e.g., survival, health gain, satisfaction). The dimension you pay attention to - and interest in - depends on whether you are a patient, a health care professional or a hospital administrator. However, these dimensions are linked and should be addressed individually, with the totality in mind. For instance: when using process measures extensively, these should have links to important outcomes to be valid. Testing of outcomes of all potential measures in patients may be cumbersome. An alternative may be to use consensus among clinical experts to screen for the most relevant issues and then test them in patients.[195]

Patients are primarily interested in the clinical outcome and seek health care services with a health problem or concern they hope to resolve. The operation per se is not the patient's goal. Further, the outcomes and results essential to the patient may differ from those important to physicians.[87,196] An example may be that members of the Delphi group regarded the selection of given medications as necessary, which were irrelevant to the patients as an outcome. Also, the patients may differ in what change(s) in outcomes they perceive as clinically important. Minimum clinically important differences (MCID) are introduced as a threshold value for such change(s), often combined with patient-reported outcome measures (PROMs). PROMs are self-reported questionnaires (generic or condition-specific) to ascertain the patients' perceptions of their health status. We can also use them to evaluate the effectiveness and safety of an intervention.[196]

The choice of objective clinical outcome indicators is also of importance. For example, in the U.K., the National Health Service reports on the proportion of patients recovering to their previous mobility /walking ability levels at 30 days and 120 days after hip fracture. Presently, in Norway, we get reports only on 30-days mortality after hip fracture. (https://digital.nhs.uk/data-and-information/publications/statistical/nhs-outcomes-framework/december-2020-supplementary-release)(Helsedirektoratet (2019).

Hoftebrudd - overlevelse 30 dager etter innleggelse [nettdokument]. Oslo: Helsedirektoratet https://www.helsedirektoratet.no/statistikk/kvalitetsindikatorer/behandling-av-sykdom-og-overlevelse/overlevelse-30-dager-etter-innleggelse-for-hoftebrudd)

The development of constantly improved surgery, anaesthetic procedures and treatment in PACUs allows even more patients to be offered surgical treatment. This development continually pushes the limits for age, concomitant illness and physical fitness for acceptance to surgical procedures and subsequent anaesthesia. The PACU is often a bottleneck for hospital logistics, being personnel- and equipment-intensive. For most hospitals, the substantial reduction in the level of care from the PACU to the ward regarding staffing, monitoring and surveillance may increase the risk for the patients. As shown in Paper I, patients need frequent adjustments in follow-up during the first 24 postoperative hours. Likewise, shown in Paper II, patients benefit from a frequent clinical evaluation postoperatively as this may reveal quality deficiencies with potential patient harm.

5.4 Limitations

In study 1 B, we had few patients with complications which is a limitation in detecting safety issues and establishing a high sensitivity valid for a large population. It is also a limitation that there was a bias with many female and elderly patients undergoing planned orthopaedic surgery and many ASA 1- and 2 - patients. In addition, the observation period was limited to 24 hours, and we did not do follow-up and clinical outcome evaluation of patients with high ESS or extensive evaluation of treatment given. Further, the ESS was tested as a whole and not in its five domains separately.

In study 2, we included the prostatectomy patients with mobility restrictions, which led to clustering and a decision not to include these patients for this outcome. This situation resulted from deliberately selecting one *ward* as the basis for the study and not selecting specific patient groups suitable for research purposes only.

We did not establish our baseline values for the patients in study 2 arriving in the ward but used the PACU discharge criteria as the predefined baseline. This is a limitation to detecting clinical changes for each patient from the admission status, although we obtained the first set of values within the 1st hour of ward admittance. Similarly, we did not record a preoperative assessment of pain and analgesic medication, which will influence the

postoperative status and clinical outcomes,[197] although similarly in the two randomised groups.

It is a limitation of this study that we chose to combine the ESS and WPM and hence did not investigate the effects of the components separately. Other limitations for study 2 are the relatively limited observation period and a too low number of patients to prove potentially improved safety. As all patients were discharged to the ward based on fulfilling a checkout list before becoming a part of this study, we expected a low frequency of serious complications. Anticipated low risk of further serious complications is an essential pre-requisite for being discharged to the ward, irrespectively of ASA classification. In addition, many ASA 3 or 4 patients will spend the first night at the PACU or even some in the ICU unit, which will not make them eligible for inclusion within the 0-24 postoperative period scope used in our studies.

A legitimate question regarding patient satisfaction is whether the observed differences are just because of better pain treatment, not the ESS. Furthermore, we did not have a blinded intervention in study 2. The study was known to all involved with the parallel groups, and this may have affected the care provided for the control group. It is a limitation for study 2 that we only tested in one ward, contrary to multiple wards in study 1 B and study 3.

A limitation of study 3 is that we did not record the total surgery time and dosage of anaesthetics during surgery, and it is unclear whether they were comparable across all participants. We noticed no significant differences between the groups regarding demographic variables such as age, BMI, gender, ASA classification, and type of anaesthesia in the hospital of Astana. The demographic differences between the groups at the University Hospital of Krasnodar may be considered a study limitation. In order to avoid the effects of differences in ASA classification, type of surgery, and anaesthesia, we also selected and analysed additional data from subgroups of patients operated with laparoscopic cholecystectomy in the two hospitals. Also, in these subgroup analyses, the LOS was significantly shorter in the ESS group than in the control group. As mobility degree and morbidity displayed no significant intergroup differences, we could not identify the precise mechanism contributing to LOS reduction in the ESS group. Finally, the lack of blinding of the intervention procedures can also be considered a limitation of this study.

6. FUTURE PERSPECTIVES

"*Improvement begins with I."* Arnold H. Glasow

The knowledge about the quality issues in handling postoperative pain and its side effects is good but needs a higher priority. The unquestionable medicolegally and ethical aspect of adequate relief of severe postoperative pain will still be present and will not "disappear and be forgotten" soon after a successful surgical procedure[198]. However, it should be safer and easier to initiate needed pain treatment instead of leaving the patient with discomfort due to limited possibilities of proper follow-up. We need to focus on postoperative treatment as part of future patient-centred health care,[194] which means acknowledging each patient's needs in the perioperative setting and making individual adaptions to treatments and follow-up in all phases of the hospital stay.

Redundancy in the wearable technical solutions with multiple sensor parameters and automated trend and pattern recognising are areas of future development, so deteriorating patients can be identified even before any single value reach the alarm threshold.[152]

The technical solutions for wireless and bedside assessment and documentation of patient status are being introduced now, hopefully with an increasing application in times to come. Wearables for patient monitoring are becoming increasingly available,[152] but the costs, logistics and technical infrastructure are obstacles to widespread introduction. A review from September 2021 states: "The ideal mobile monitoring system for ward patients should continuously measure all relevant vital signs, including SpO_2 and blood pressure; should not interfere with daily activities; and should be highly resistant to motion artifact. Such a system does not exist yet." [167]

Vital sign monitoring is rarely sufficient to diagnose a specific disease or complication. Solely "fixing" abnormal vital signs, e.g., providing extra oxygen for low arterial pulse oximetry, is unlikely to be the best treatment. Specific treatment should be contextualised and personalised to improve outcomes.[108,199] Indeed, regarding postoperative pain, this is also of uttermost importance, as a cause for undue strong pain should always be looked for before more analgesic is given. Future use of the ESS may be a clinical tool complementing and included in a robust, reliable and redundant system for postoperative surveillance.

Implementing continuous monitoring systems on the ward for postoperative surveillance must not become an incentive to discharge patients prematurely from overcrowded PACUs. Neither should such systems warrant keeping deteriorating patients on the ward if needing a higher level of care.

7. CONCLUSIONS

"After all is said and done, more is said than done". Aesop

This thesis extends previous knowledge of postoperative pain treatment and the dynamics of the patients' needs in the first early postoperative phase on the ward.

This thesis aimed to develop and implement a new tool for improved and efficient pain management of postoperative patients on the surgical ward while ensuring and maintaining optimal patient safety. The tool should help identify postoperative patients in need of more accurate and specific treatment.

We have answered these aims through three papers. First, we identified clinical outcome variables of major importance for the postoperative ward patients' status regarding safety and perceived quality of care. These outcome variables were then transformed into simple measurements and summarised into a new clinical score, the Efficacy Safety Score (ESS). The ESS fulfils the established criteria for score quality validation and adequately reflects the patient's postoperative recovery status with high sensitivity. Furthermore, we have shown that using the ESS combined with wireless patient monitoring may improve postoperative patient quality issues: more targeted pain management, less pain, increased satisfaction, and more rapid mobilisation, with shortened length of hospital stay and maintained safety.

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9. PAPER I

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RESEARCH ARTICLE Open Access

Development and validation of the Efficacy Safety Score (ESS), a novel tool for postoperative patient management

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Abstract

Background: Several reports have shown that postoperative monitoring of general safety and quality issues, including pain treatment, after discharge from recovery is often non-systematic and inadequate. We suggest a new score with assessment of key recovery parameters, as a supportive tool for postoperative care and a call-out algorithm for need of extra help. The aim of this investigation was to validate the score.

Methods: After suggesting a prototype score from a pilot study in 182 postoperative patients, we performed a Delphi process by using international experts to create consensus on the final score contents and called the revised tool the Efficacy Safety Score (ESS). Then, we performed a prospective observational study with the ESS throughout the first 24 h postoperatively in 207 surgical in-patients. We compared ESS with Modified Early Warning Systems (MEWS), and postoperative journal information. We subsequently validated ESS by addressing recognized quality criteria for measurement of health status questionnaires.

Results: A call-out value of ESS ≥10 correlated with MEWS > 0 values and journal information about postoperative concerns with a sensitivity of 94% and 92%, respectively. All serious safety issues were identified with the ESS ≥ 10, and a higher number of quality issues were identified than with routine care or MEWS. We obtained positive ratings for six out of seven tested criteria of questionnaire quality; one criterion had an indeterminate rating.

Conclusion: ESS fulfils suggested criteria for score quality validation and reflects the patient's postoperative status adequately and with high sensitivity. Further clinical trials are warranted to evaluate the usefulness of ESS as a simple tool for assessment of the postoperative safety and quality of patients.

Keywords: Postoperative care, Postoperative pain, Postoperative nausea and vomiting, Call-out algorithm, Checklist

Background

In modern perioperative care, safety is a primary concern, although in-hospital mortality in a large, mixed surgical French adult populations recently was reported to be as low as 0.5% [1]. Much more frequent, although less serious, are the problems of patient perceived quality, especially in the post-operative period.

In a survey of 2252 patients, 55% reported that they suffered from unsatisfactory pain treatment postoperatively [2]. Even so, a considerable number of patients experience adverse effects of the analgesic treatment given. A recent review including data from 183 studies comprising more than 100.000 patients undergoing postoperative pain treatment, showed a high incidence of side-effects from pain treatment: 25% suffered from nausea, 20% from vomiting, 15% from pruritus and 23% from urinary retention, whereas no cases of serious respiratory depression were reported. Notably, still 24% of the patients received too little analgesia for their pain, and only 2.6% were classified as receiving too much analgesics or sedatives [3]. Side effects are most typically opioid - induced. Thus, it may be argued that health care personnel should aim at better surveillance of peri-operative quality, both analgesic effects and side-effects.

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A universal postoperative registering system for quick analysis of the overall safety, quality and efficacy by the same tool may create a higher level of confidence and security within the nursing staff. Moreover, lack of feedback on the analgesic effects or fear of side-effects of especially opioid administration, may lead to under dosing, whereas improper non-systematic monitoring of side-effects may lead to overdosing. Cases of fatal outcomes in hospital as well as at home after discharge has been described in this context [4–8].

As long as the patients remain in the post-anaesthesia care unit (PACU) with continuous monitoring and observation by highly trained staff, there are abundant tools and measures at hand to ensure both safety and quality of the treatment. However, after discharge to an ordinary ward, there are less staffing and monitoring resources, and the patients may even be left alone for shorter or longer periods of time.

Other scores available for postoperative assessment are usually designed for a specific purpose and not a global longitudinal evaluation. Examples include score for readiness for PACU discharge (e.g. the Aldrete score), score for the long-term outcome and patient satisfaction (e.g. PQRS) or score for acute medical deterioration (e.g. MEWS). We were looking for a clinical tool to address longitudinal quality and safety in combination, as a routine audit for every postoperative patient, with a special focus on the time period from PACU check-out to discharge readiness from hospital.

We hypothesized that medical personnel responsible for postoperative care and pain treatment, especially at the ward, but also in the PACU, may benefit of the feedback from a simpler, but still complete, scoring system. The system should survey safety aspects of changes over time in consciousness, respiratory and circulatory parameters as well as patients' subjective postoperative perceived quality, including effect of pain treatment and side effects. The scoring system should include a call-out algorithm for the nursing staff to get help and guidance from the physician on call.

For this purpose, we started with an algorithm-based monitoring system with multiple simultaneously recorded variables, as a prototype tool for assessment of quality and safety of postoperative treatment [9, 10]. After a successful pilot, we decided to develop this tool further through a proper consensus, documentation and validation process. The goal of the present investigation and report is to present the results of this development and validation.

Methods

The Regional Committee for Medical and Health Research Ethics South East evaluated this observational prospective study part of the validation process as a quality assessment exempt from informed consent of the patient (ref 2014/580 A). The patient protocol was approved by the Local Data Inspectorate of Vestre Viken Hospital Trust, Drammen, Norway (ref 2015/4793) who is the owner and administrator of Kongsberg Hospital.

We address four aspects of the validation process:

1) Based on the prototype score and a Delphi process [11] with a panel of recognised experts, we sought to obtain consensus on the contents of the score, which after revision was called the Efficacy Safety Score (ESS).
2) We validated ESS in a new group of patients encompassing independent scoring by two nurses.
3) Since no unified previous tool existed which could be compared with the whole score, we compared ESS with the modified Aldrete score [12] and the Modified Early Warning Score (MEWS) [13], which have a focus on the safety aspects of recovery.
4) Finally, we evaluated the ESS as to quality criteria proposed for the validation of health status questionnaires by Terwee and co-workers [14].

Development of the score tool

Table 1 shows the different steps in the process of developing the postoperative score tool towards the ESS version, which then were validated. Initially, we searched the literature and found several postoperative assessment scores [12, 15–22]. Since we found no simple system constructed for global monitoring of the general status, as well as efficacy and side - effects of pain treatment after discharge from PACU, we developed a prototype score tool, "the Kongsberg satisfaction score", (KSS) for this purpose. The prototype was based on

Table 1 Steps in the process of developing Efficacy –Safety Score (ESS)

Steps	Process
1.	Comprehensive literature review to identify current postoperative scales and scores to determine their limitations.
2.	Identification of aspects of interest regarding postoperative patients based on empirical experience.
3.	Pilot study ($n = 182$) with the prototype score to identify possibilities and pitfalls for a novel tool for postoperative use [9, 10].
4.	Identification through a Delphi-project the aspects considered relevant for clinicians to make a postoperative assessment [11]. Table 2.
5.	Refining the score and system after pilot study and Delphi-project.
6.	Writing of a protocol and conducting of a validation study in 207 patients.
7.	Validation of the ESS against the criteria set by Terwee et al. [14] Table 4.

information about consciousness, postoperative nausea/vomiting (PONV) and the degree of experienced pain at rest and during mobilization using Verbal Numeric Rating Scale (VNRS) [23]. We intended to make the score simple and easy to perform, facilitating the everyday use on all postoperative patients. This also includes baseline aspects related to regional anaesthesia, including neuraxial blocks. Still, in these situations there are some specific issues of nerve block characteristics and safety issues which are specific and different depending upon the type of regional anaesthesia. In order to maintain a simple, universal and quick to use all-purpose score, these specific aspects of different regional anaesthesia techniques are not included in our score, but should be added to the use of ESS on an individual case bases.

The prototype score tool was tested on a pilot population of 182 patients, previously reported [9]. In parallel with testing the prototype score tool, we performed a modified Delphi-process with three iterations until consensus. An international group of ten recognized experts in postoperative care made suggestions about information needed in order to give an adequate and sufficient evaluation of the state of the clinical condition after discharge from PACU. Consensus was pre-defined as more than 80% agreement between the participants. The result of this process, shown in Table 2, was used to revise the prototype score from the pilot-study, as the issues of consciousness and general condition was added into the ESS for the subsequent validation study.

Depending on the patient's status or complaints, each of the clinical features in the final version were scored from 0 to 15 and summarized in a total score (Table 3). From the pilot study it was suggested that an ESS score ≥10 was an appropriate cut-off value for serious problems in need of immediate consultation with a doctor or other expert health personnel. The project group discussed at which single events (such as respiratory or cardiovascular problems) or combination of minor events a clinical intervention was needed. It came out that single serious events or combination of minor events with score of more than 10 seemed to be a reasonable cut-off point to test. However, the study was designed to reconsider retrospectively the cut-off point in case of some serious events were missed by this cut-off point (i.e. cut off point should be lower), or too many false calls for intervention was initiated (i.e. cut off point should be higher). For this reason, the cut-off value of ≥10 was tested prospectively, allowing for a post-hoc evaluation of the proper cut-off value.

Table 2 Arrangement and results of Delphi-process

Questions in modified Delphi process	Answer given with consensus, >80% concordance, $n = 10$. (% agreement).
1. To make a judgment of a patient's postoperative condition during the first 24 h after surgery, what clinical information do you need?	✓ Blood Pressure (100) ✓ Breathing Frequency (100) ✓ Pain (100) ✓ Pulse Frequency (100) ✓ Diuresis (90) ✓ Level of Consciousness (90) ✓ Nausea (90) ✓ Oxygen Saturation (80)
2. How will you assess and enter a patient's pain postoperatively?	✓ Numeric Rating Scale/Visual Analogue Scale at rest (100) ✓ Numeric Rating Scale/Visual Analogue Scale during movement/coughing (100)
3. How will you assess and enter the degree of mobilization of a patient after surgery?	✓ Mobilized in bed/sitting in bed (100) ✓ Walk some steps with/without support (100)

Table 3 Description of Efficacy Safety Score (ESS) as revised after pilot-study and Delphi-process

Mental status	Score
Awake and alert patient	0
Awake patient, but influenced by drugs. Difficulties in communication.	5
Acutely confused, upset/uneasy, hallucinated or euphoric patient	10
Unresponsive patient	15*
Postoperative nausea and vomiting (PONV) status	
No postoperative nausea or vomiting	0
Postoperative nausea only	5
Postoperative nausea and vomiting/retching	10
Pain status at rest	
No postoperative pain	0
Low intensity postoperative pain (VNRS 1–3)	1–3
Moderate intensity postoperative pain (VNRS 4–6)	4–6
Severe intensity postoperative pain (VNRS 7–10)	7–10
Pain status during movement	
No postoperative pain	0
Low intensity postoperative pain (VNRS 1–3)	1–3
Moderate intensity postoperative pain (VNRS 4–6)	4–6
Severe intensity postoperative pain (VNRS 7–10)	7–10
General condition status	
No remarks	0
Minor discomfort (e.g. light-headedness, minor itching, blurred vision, decreased urination etc.)	5
Excessive discomfort (e.g. severe dizziness, itching, restlessness, urine retention, sensation of cold/warmth, cold sweating)	10
Acute circulatory abnormalities (blood pressure ≤80 or ≥200 mmHg, heart rate ≤40 or > 110)	15*
Acute respiratory abnormalities (dyspnoea, respiration rate < 9 or >20/min, long pauses in breathing, shallow breathing)	15*

*Any single score of 15 (on either consciousness, circulation or respiration) should call for IMMEDIATE activation of acute assistance with the patient

Validation study

A prospective observational study was conducted at Kongsberg Hospital to monitor postoperative in-patient status with the ESS during the first postoperative 24 h to provide data to validate the ESS score against published general criteria for validation of verbal scores set out by Terwee et al. [14] (ref. Table 4). Data were collected between March and August 2015 at the Departments of Anaesthesiology, High dependency Unit, General Surgery, Orthopaedics, Obstetrics and Gynaecology, and Ear-, Nose- and Throat at Kongsberg Hospital, Kongsberg, Norway.

a) Prospective clinical study:

ESS was used by the regular staff at the ward after education was given. The registration chart was on paper sheets and filled in by nursing staff hourly the first 8 h postoperatively (also including the PACU period), and then every 4 h for the next 16 h at the ward. The highest score in each time period of 1 h in the PACU and 4 h at the ward was registered.

The inclusion criteria were all operated patients who were expected to be treated and observed in hospital overnight. Exclusion criteria were patients < 18 years of age or patients with poor communication capabilities.

Table 4 Terwee et al. quality for health status questionnaires

1. Content validity	The extent to which the concepts of interest are comprehensively represented by the items in the questionnaire
2. Internal consistency	The extent to which items in a (sub)scale are inter-correlated, thus measuring the same construct
3. Criterion validity	The extent to which scores on a particular questionnaire relate to a gold standard
4. Construct validity	The extent to which scores on a particular questionnaire relate to other measures in a manner that is consistent with theoretically derived hypothesis concerning the concepts that are being measured.
5. Reproducibility	a. Agreement The extent to which the scores on repeated measures are close to each other (absolute measurement error) b. Reliability The extent to which patients can be distinguished from another, despite measurement errors (relative measurement error)
6. Responsiveness	The ability of a questionnaire to detect clinically important changes over time.
7. Floor and ceiling effects	The number of respondents who achieved the lowest or highest possible score.
8. Interpretability	The degree to which one can assign qualitative meaning to quantitative scores.

b) Quality assurance based on individual patient data:

In parallel, we collected several parameters from the complete journal of the patient (Table 5), in order to check if important information from the regular routine monitoring and registration was missed in the ESS registration of the individual patients. From the PACU stay we checked the charts of regular PACU monitoring on vital signs and medication, as well as the fulfilment of PACU discharge criteria form by the modified Aldrete score [12]. At the ward, we used the Modified Early Warning Systems (MEWS) [13], applied on the scheduled nursing notes to validate the ESS. The MEWS is a validated tool developed to identify patients with acute deterioration, including four physiological measurements (i.e. systolic blood pressure, heart rate, respiratory rate, temperature) and one observation (level of consciousness), with a total score from 0 to 14.

c) Validation of the ESS score (see criteria in Table 4 and Additional file 1: Addendum 1):

For formal validation of the ESS we used "The Quality for Health Status Questionnaires criteria" listed by Terwee et al. [14] as a guide for the process. These criteria are explicit requirements for formal validation of questionnaires. The detailed descriptions of the criteria are given in Additional file 1: Addendum 1.

Statistical methods

All collected data were registered in Microsoft® Excel® 2010 for PC, version 12.0. Patients were ASA classified and sorted in groups according to the type of surgery and anaesthesia. The results are given as numbers and percentages for selected groups, and as means ± standard deviations (SD) for age, weight, height and Body Mass Index (BMI). Statistical analyses were conducted using IBM® SPSS® Statistics Version 21 for one-way Analysis of Variance (ANOVA), estimating Intra-class Correlation Coefficient (ICC) and post-hoc Bonferroni correction. For between-group differences when the data were

Table 5 Information extracted from cohort medical journals

1. Information about pain, nausea and vomiting the first 24 postoperative hours
2. Information about medication given the first 24 postoperative hours
3. Time to readiness for discharge from recovery unit (Modified Aldrete Score ≥9)
4. Not-scheduled contacts/visits by physician
5. Re-admittance to high dependence unit or re-operation
6. Result of performed Modified Early Warning Score at the ward
7. Time spent at recovery unit, total hospital stay and 30-days mortality

compared by gender and ASA-score, we used repeated-measures ANOVA.

Results

We enrolled 207 patients scheduled for inpatient surgery for validation of the ESS. Two patients were excluded due to age under 18. The demographic details for the cohort are shown in Table 6.

Evaluation of measurement properties criteria:

Content validity

After the modified Delphi-process, in which we regarded agreement between the experts of 80% or more as consensus, we adjusted the prototype score into the ESS, for subsequent validation study (Table 3).

Table 6 Demographics and operative variables in cohort, $n = 207$

	Range	Mean (±Standard Deviation (SD))
Age, yr	18–92	57,9 (±16,4)
Height, m	1,50 – 1,98	1,69 (±0,09)
Weight, kg	40–160	77 (±15,7)
Body Mass Index (BMI)	17,2–37,6	27,0 (±4,9)
Duration of anaesthesia, min	29–210	107 (±57)
	n	Percent
Gender, female	165	79,7%
American Society of Anesthesiologists Status:		
ASA I	71	34,3%
ASA II	112	54,1%
ASA III	22	10,6%
ASA IV	2	1,0%
Planned Surgery	178	86,0%
Type of surgery		
Orthopaedic - total	99	47,8%
Knee/total hip joint replacement	28 / 50	13,5% / 24,2%
Fracture fixation	19	9,2%
Other	2	1,0%
Gynaecological - total	94	45,4%
Vaginal/open hysterectomy	37 / 7	17,9% / 3,4%
Laparascopic hysterectomy	22	10,6%
Vaginal repair surgery	16	7,7%
Caesarean section	8	3,9%
Other	4	1,9%
Ear, nose and throat - tonsillectomy	14	6,8%
Type of anaesthesia		
"Target"-control infusion(TCI) of propofol and remifentanil	94	45,4%
Spinal anaesthesia(SA)/Epidural anaesthesia(EDA) ± sedation(sed)	73 / 2	35,2% / 1,0%
TCI + EDA/Regional block(RB)/SA	28 / 2 / 2	13,5% / 1,0% / 1,0%
Gas anaesthesia(GA): sevoflurane and fentanyl	6	2,9%

The ESS is built up from already clinically validated domains: Four level judgement of mental status, 11-point numerical pain assessment and MEWS in general status. Digitalized expressions from these domains are incorporated into one simple tool together with clinical assessments of subjective comfort/discomfort for the postoperative patient. These individual domains are all related but independent factors to the clinical status of patients in the postoperative phase, see Table 7.

Internal consistency

Not relevant for ESS (see methods).

Criteria validity

ESS and discharge from PACU checkout

The PACU discharge criteria used in the study hospital were the modified Aldrete score ≥9 [12] in addition to registration of none or mild pain (VNRS ≤ 3) and absence of postoperative emetic symptoms. The study hospital routinely recorded the time of complete achievement of all criteria, without specific notes on the individual criteria. The mean ESS at the time of fulfilling these criteria was 2.84 (SD 2.82).

ESS versus MEWS

In the 16 patients (8%) with a positive MEWS score (1 to 5), we found a correlation with ESS ≥ 10 for 15 patients (sensitivity against MEWS = 0.938). The one patient with positive MEWS and ESS < 10 presented with tachypnea (rate 20/min), without clinical implications. There were no patients with a positive MEWS in the remaining 106 patients (51% of sample) with ESS ≥ 10 (specificity against MEWS of 0.445).

ESS versus patient journal information

A total number of 121 patients (58%) had an ESS score of ≥10, as an indication of a relevant safety or quality problem. A total of 99 patients had a note in their journal about postoperative concerns; such as pain, nausea, vomiting, circulation irregularities, respiration remarks and/or notes on general condition. Ninety-one of these patients had an ESS ≥10. Eight patients had ESS < 10 where of 6 with minor issues not being significant safety concerns; two patients had episodes of nausea, one of anxiety, two of moderate "dull" pain and one of disorientation. Two potential safety issues were missed by the ESS, probably due to missing ESS registrations for the relevant period of their recovery: one had bradycardia (42beats/min) and one had tachycardia (115beats/min). Of the remaining 91 patients with a postoperative note on either safety or quality issues in their journals and concomitant ESS ≥10, we found three patients with syncopation -, one with apnoeic periods after opioid administration -, four with tachycardia >129/min, two

Table 7 Mean values (SD) of Efficacy Safety Score (ESS) and mean values of individual domains deconstructed, $n = 207$

Postoperative hours	1	2	3	4	5	6	7	8	12	16	20	24
ESS	5.5 (7.4)	3.9 (4.6)	3.7 (4.4)	3.6 (4.5)	3.8 (4.5)	3.7 (4.3)	4.0 (4.2)	4.2 (4.2)	4.6 (5.8)	3.7 (4.5)	3.9 (4.4)	3.7 (4.0)
Mental status	0.5 (2.0)	0.1 (0.9)	0.1 (0.9)	0.0 (0.4)	0.0 (0.4)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.1 (0.3)	0.0 (0.0)	0.0 (0.0)	0.1 (1.0)
PONV	0.4 (1.5)	0.5 (1.7)	0.6 (2.0)	0.3 (1.5)	0.4 (1.6)	0.5 (1.8)	0.6 (1.9)	0.6 (2.0)	0.,5 (1.8)	0.4 (1.5)	0.5 (1.8)	0.3 (1.4)
Pain status at rest	2.0 (2.8)	1.5 (2.0)	1.3 (1.6)	1.4 (1.6)	1.4 (1.7)	1.3 (1.6)	1.4 (1.5)	1.5 (1.8)	1.6 (1.8)	1.4 (1.8)	1.4 (1.5)	1.1 (1.2)
Pain status during movement	2.0 (2.8)	1.6 (2.1)	1.5 (1.8)	1.7 (1.8)	1.7 (1.8)	1.7 (1.8)	1.8 (1.7)	2.0 (2.0)	2.0 (2.1)	1.8 (2.1)	1.9 (1.9)	1.9 (1.9)
General status	0.6 (2.1)	0.2 (1.3)	0.2 (1.0)	0.2 (1.3)	0.3 (1.7)	0.2 (1.4)	0.2 (0.9)	0.1 (0.7)	0.3 (1.7)	0.2 (0.9)	0.2 (0.9)	0.3 (1.7)

with systolic blood pressure <90 mmHg and two in need of extra oxygen supply because of $SaO_2 < 90\%$. For the remaining 79 patients there were relevant quality issues, but no aspect of safety problems involved.

The overall sensitivity for this comparison of ESS ≥10 against relevant journal information was 0.919 and the specificity was 0.722.

Construct validity and responsiveness

For the sub-group having total joint replacement ($n = 78$) the mean ESS for the first two hours was 1.5 (±2.4) and 8.7 (±6.6) for regional anaesthesia and general anaesthesia, respectively. Estimated mean difference was −7.2 (95% Confidence intervals (CI) 5.17–9.23, $P < 0.0001$) in significant favour of regional anaesthesia.

For the gynaecological hysterectomy sub-group ($n = 66$), the mean ESS for the first 2 h was 4.7 (±4.4) and 7.4 (±6.2) for regional anaesthesia and general anaesthesia, respectively. Estimated mean difference was −2.7 (95% CI 0.04–5.36, $P = 0.0466$) in significant favour of regional anaesthesia for this sub-group.

This confirms the ability of the ESS to significantly differentiate two groups of expected different recovery quality in two different subpopulations. Looking at individual differentiation is not clinically relevant as the patients with best recovery safety and quality in the general anaesthesia group will be expected to overlap with the patients with most recovery problems in the regional anaesthesia group.

Reproducibility

Reliability

The estimated ICC from the reliability testing was 0.953. This value is larger than 0.70, which was suggested for positive rating by Terwee et al. [14].

Agreement

The estimated SEMagreement is 0.197 (SEMagreement = SD x (√1-ICC)). Estimated SDC is 1.26 (SDC = 1.96x √2x SEMagreement). This SDC is less than the defined MIC of 1.30 and the statistically estimated MIC of 2.33, as described under interpretability, which gives a positive rating according to Terwee et al. [14].

Floor and ceiling effects

The theoretically possible highest ESS is 60, and no patient in the cohort approached this value. Floor effect, ESS = 0, which is the patient's habitual situation of 100% well-being, was found in 4.8% (10 patients) for the whole observation period of 24 h.

Interpretability

The standard deviation of the ESS for the cohort at all time points was 4.65. Correspondingly MIC is 2.33, estimated by the distribution method. Two significant subgroup effects were identified: this involved the variables age and type of anaesthesia. Bonferroni post hoc testing showed the effect to be located between the patients aged ≤65 or ≥75 years, respectively, at the 1st and 24th hour postoperatively. Effect was also shown to be located between the general anaesthesia versus the regional anaesthesia groups at the 1st, 2nd and 16th postoperative hours, Fig. 1. We found no significant between-group differences when the data were compared by gender and ASA-score.

Discussion

In this study on the validation of our newly developed ESS score, we found the score sensitive and useful in routine postoperative care. Our pre-set call-out value greater or equal than 10 for calling for enforced attendance and help, seemed to be appropriate for further testing as no cases of serious events were missed by this call-out value. Although 51% of all patients qualified for the need of physician attendance by this call-out value, we think it is important to be on the safe side. It is better with some calls not being needed, than missing one urgent and important case. Also, in 88% of the call-outs there was a significant quality problem of patient care which should justify the involvement for the physician on duty.

With the ESS we addressed and fulfilled the seven relevant out of total eight validation criteria recently suggested by Terwee et al. [14]. Positive rating was assigned for six of the criteria, and an indeterminate rating was assigned for the final criterion of validity due to the lack of convincing arguments that the suggested gold standards are definite as such.

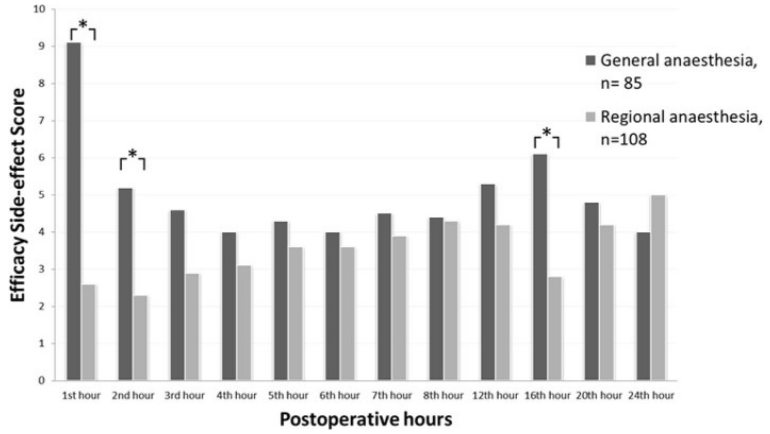

Fig. 1 Mean values of Efficacy Safety Score (ESS) for subgroups of regional versus general anaesthesia during the first 24 postoperative hours. *P=0.05

When developing health-status questionnaires, no empirical evidence exists concerning the final choice of quality criteria. The criteria suggested by Terwee et al. [14] are based on those of the Scientific Advisory Committee of the Medical Outcomes Trust [24]. Still, the Terwee et al. [14] checklist is not itself a gold standard to determine quality of a questionnaire, and the checklist does not determine which is the best questionnaire in an everyday clinical situation. The checklist is however recognized as a tool, which provides a systematic review of measurement properties to rate the quality of a questionnaire or test-battery, and considered helpful when introducing a new scoring system.

It is important that the use of the new scoring system never result in any delay in emergent situations when patient's safety is acutely threatened. For this reason, any one of the three observations on: unconsciousness, acute circulatory problems or acute respiratory problems is designated a score of 15, which should call for immediate actions as to get qualified help.

For the quality part of the ESS related to pain and nausea/vomiting/retching, the scaling is based on the well-established verbal 11-point numerical scale (0–10) used for assessment of pain [23]. Postoperative pain is a major concern for patients after surgery, and this is reflected in the score by evaluating pain both at rest and at movement, also because mobilization is an essential aspect of recovery after surgery. We regarded unconsciousness as a condition being more concerning from a safety point of view than severe pain and vomiting/retching, and gave consciousness a score range from 0 to 15. The same considerations were made for circulatory and respiratory abnormalities.

The empirical weighting of the different aspects of the score may be questioned, but the purpose of the score is to give the nursing staff a quick and simple tool in analysing the patient's postoperative status. It does not include all aspects of postoperative care, and is not designed to explore in detail the degree of severity of the patient's condition. It consists of specific aspects of recovery problems summarized to a single number as a call-out algorithm. It is made to identify patients who need their care adjusted in a busy daily care. The goal is to make a simple judgement of every patient with specific questions on clinical concerns important for the postoperative patient. When performed in daily clinical situations, the score is deconstructed into these individual domains and the staff can make clinical decisions from this. We have data from patients having high ESS due to severe postoperative pain, which continues having high ESS after the pain is treated, but now side-effects like retching and vomiting is the cause. This balanced clinical approach to the patients with explicit questions about all the domains is what contributes to ESS as a clinical tool, where summarized input from all the domains reflects the clinical situation. Retrospective extraction of individual domain data helps to analyse postoperative care retrospectively, and may improve quality of care.

We consider the low specificity under criteria of validity with comparison to MEWS to be due to the different aspects and aims of the two scores. The ESS reflects the quality and safety of the treatment given postoperatively in a wider scope and with a sensitive scaling, whereas the MEWS is constructed for safety issues primarily, with a simple dichotomous "no problem" versus "serious problem" score.

As to comparison of ESS with information in the medical journal, the latter is often sporadically and non-methodologically written. Still, all serious problems will be reported in the journal, either as such or as notes of the doctor being called upon, or extra drugs being given. The findings of very few minor clinical complaints documented in the medical journal, may explain the sub-optimal specificity for this comparison.

The ESS scores peaked at 16 h registration for general anaesthesia, whereas the opposite (i.e. low values) were shown for regional anaesthesia. This may have to do with the resolution of regional blocks at this time for many patients, with subsequent pain and administration of systemic analgesics with some side-effects. In the general anaesthesia group, it may have to do with the morning round at the ward, topping up analgesic treatment.

In a recent review, Bowyer and co-workers identified 11 different scoring tools of recovery status, checking and documentation. Out of those the authors concluded that the Postoperative Quality of Recovery Scale (PQRS) was best in assessing recovery in all relevant domains, including physiological, nociceptive, emotive, activities of daily living, cognition and patient satisfaction [25]. It addresses recovery over time and compares individual patient resumption of capacities data with base line, and is an acceptable and appropriately validated method for identification of individual patient recovery. However, as the PQRS is designed with 22 questions to cover all aspects of the full post-operative course, from leaving the operating room until full resumption of normal activities, it is perceived as cumbersome and time consuming to use. Further, it necessitates a baseline registration in order to make proper value to the dichotomous outcome of either worse or similar/better as compared with the pre-operative status. For these reasons, even the authors suggest PQRS basically as a tool for research, not for everyday clinical practice [15].

Other scoring systems are also available and extensively used, such as the MEWS system [13] and the Aldrete score [12]. The MEWS system is a simple system on safety issues only, and does not take into account quality aspects. This was also evident in our test of the MEWS versus ESS in the present study.

The Aldrete score is specially designed as a dichotomous "yes" or "no" tool for PACU discharge, with no grading of safety and quality issues. Further, it does not take into account the longitudinal progression of postoperative status with time.

After the prospective study an evaluation report was written by the nurses about ESS. The report described improved communication and it emphasized that the call-out algorithm made it easier to get immediate help and assistance for postoperative patients.

Limitations of the study

It is a limitation of this study that the observation period for ESS only was for the first 24 postoperative hours. This was chosen in order to focus on safety problems, which are more frequent during the first 0–24 h, for the important sensitivity of the scoring system on this aspect. A further limitation is that data described in this paper reflects the cohorts and surgical case load in the hospital studied. There was a bias towards many female and elderly patients going through planned orthopaedic surgery. It may also be a weakness of the study that most of the surgery performed was planned, and that most patients had ASA status 1 or 2. While obviously the ESS will change upon efficient treatment of e.g. overt nausea or strong pain, this aspect was chosen to not be included in this first report of the score for sensitivity and specificity. A single study like this is not sufficient to claim complete clinical validation for the ESS, but it is useful for evaluating feasibility, and to check whether the score detects what it is supposed to.

Conclusions

ESS is constructed to give the nursing staff sufficient clinical relevant information about postoperative patient status and thereby a possibility to improve patient safety and enhance quality. Also, to provide a call-out algorithm (i.e. ESS >/= 10) for immediate call for competent guidance and help. ESS is a simple scoring system to apply, routinely conducted in less than one minute, making it a useful tool for the staff in regular everyday situations. It is based on clinically information that is easy accessible, and minimal training is needed prior to use. The findings from this validation project indicate that ESS may contribute positively to the field of postoperative management. ESS fulfils suggested criteria for score quality validation and reflects the patient's postoperative status adequately and with high sensitivity. However, in order to evaluate the usefulness of ESS in everyday practice and beyond 24 h hospital stay, further clinical trials are needed. The next step will be to test the sensitivity and specificity of the ESS in large patient populations, including seriously ill, patients, emergencies and major surgical cases. Also, to test if use of the score may result in better patient safety and satisfaction, as well as being perceived as useful in an everyday setting by the clinical staff.

Additional file

Additional file 1: A detailed description of the criteria we used for as a guide for formal validation of the ESS, "The Quality for Health Status Questionnaires criteria" listed by Terwee et al. [14], is presented in Addendum 1. (DOCX 27 kb)

Abbreviations

ANOVA: Analysis of variance; ASA: American Society of Anesthesiologists; BMI: Body mass index; CI: Confidence intervals; EDA: Epidural anaesthesia; ESS: Efficacy safety score; GA: Gas anaesthesia; ICC: Intra-class correlation coefficient; MEWS: Modified early warning score; MIC: Minimal important change; PACU: Post-anaesthesia care unit; PONV: Postoperative nausea and vomiting; PQRS: Postoperative quality of recovery scale; SA: Spinal anaesthesia; SD: Standard deviation; SDC: Smallest detectable change; SEM: Standard error of measurement; TCI: Target-control infusion; VNRS: Verbal numeric rating scale

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Authors' contributions

ES and VK conceived the study and designed it together with JR. ES administered the study, collected and analysed the data together with VD, JR and LJB. ES, VK, JR, LJB and VD all contributed with drafting the manuscript. All authors have read, made inputs to, and approved the final manuscript.

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Availability of data and material

The datasets and/or material analysed during the current study is available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Ethics approval and consent to participate

The Regional Committee for Medical and Health Research Ethics South East evaluated this observational prospective study part of the validation process as a quality assessment exempt from informed consent of the patient (ref 2014/580 A). The patient protocol was approved by the Local Data Inspectorate of Vestre Viken Hospital Trust, Drammen, Norway (ref 2015/4793) who is the owner and administrator of Kongsberg Hospital.

Publisher's Note

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Additional file 1: ADDENDUM 1

We evaluated the below criteria according to Terwee et al [14].

Content validity

This is the ability of the score to contain and adequately ask for the relevant issues, leaving out issues, which are non-relevant for the purpose. Content validity was established by our two-step process: First, the pilot-study [9, 10] with the prototype score was based on empirical clinical experience, comprehensive literature review and a thorough evaluation of common side-effects of anaesthesia and pain treatment (table 1). Thereafter we established a Delphi-project to collect expert opinions for the topic, and incorporated this in the novel tool for postoperative assessment, the ESS. Consensus in this Delphi-project, with three iterations to ten international experts, was defined as an agreement of 80% or more.

Internal consistency

This is the issue on having a score without internal contradictions on identical issues. Given that the ESS is a score based on different aspects of rather complex clinical phenomena that do not have to be correlated, the criterion of internal consistency is not relevant [26, 27] or possible to test.

Criterion validity

This is whether the criteria for acceptable versus non-acceptable values of the questionnaire items fit with previously recognized, validated and accepted standards. We undertook three measures for this purpose. There is no validated “gold standard” for the global postoperative patient status of the whole 0-24 hrs period after surgery. Criteria used for discharge from the recovery unit to the general ward, for instance, the modified Aldrete score [12, 16], is not

formally validated in the literature, but has been used for validation purpose of the ESS. The Modified Early Warning Score (MEWS) is validated [13], but do only address serious events and patient safety, and not so much the perceived quality for the patient. We examined to which degree the scores of the ESS corresponded to MEWS. In order not to miss any events, we also examined the journals of the 207 patients to search for answers to the questions in table 5.

Construct Validity and Responsiveness

This has to do with whether the output of the tested score corresponds to reported end results, both in terms of reflecting only relevant issues (specificity or validity), and not missing cases with relevant problems (sensitivity or responsiveness). A positive rating on construct validity and responsiveness is given where specific hypotheses are formulated and at least 75% of the results are in accordance with these hypothesis [14]. For this purpose, a priori hypotheses were generated and tested regarding the relationship between the ESS and clinical outcome. From our own experience and data on nausea and pain in the literature [28], we hypothesized a lower initial ESS for patients receiving regional anaesthesia compared to patients not having regional anaesthesia for the same type of surgery. Patients who underwent total joint replacement and hysterectomy were relevant sub-groups to study for this aspect. If the ESS could confirm this hypothesis, this would be a sign of validity. To distinguish clinically important changes from measurement error, we checked if the minimal important change (MIC) was larger than the smallest detectable change (SDC) in a relevant subgroup of pain registrations. MIC was defined by using well documented results where a reduction in pain severity equivalent of mean 1.3 points or more on a Numeric Rating Scale (NRS) was clinically significant [29]. The NRS scale we used was designed to detect 1.0 as SDC. We also estimated the MIC by using the conservative distribution method, saying that MIC is at least 0.5 x Standard Deviation [30].

Reproducibility

This has to do with the test or questionnaire producing the same results when tested repeatedly on a subject in the same situation. The postoperative situation is dynamic and thereby longitudinal reproducibility is, by nature, difficult to make. However, a random investigation of 54 patients of the total sample was undertaken with the purpose of testing reliability. Two regular staff members simultaneously and independently noticed ESS during the first hours. The results were blinded for the other staff members.

Reproducibility: Reliability

Reliability has to do with the ability of the score to record different results in different patients with different status. Reliability can be measured by estimating the Intraclass Correlation Coefficient (ICC). The model chosen in SPSS is ICCagreement: Two-way random, single measure - ICC. A positive rating is given for reliability when the ICC is at least 0.70 in a sample of at least 50 patients [14].

Reproducibility: Agreement

Agreement has to do with how close the results of the repeated measurements are, by estimating the measurement error in repeated measurements. The measurement error can be expressed as the standard error of measurement (SEM) [31]. SEM agreement equals the square root of the error variance of an ANOVA analysis including the systematic difference: SEMagreement =SD x (√1-ICC). This was then converted into the Smallest Detectable Change (SDC) using the formula SDC=1.96 X √2 X SEMagreement [32]. A positive rating for agreement is given when SDC is smaller than the defined Minimal Important Change (MIC) [14].

Floor and ceiling effects

If too many patients either have the minimum or maximum score, this might be an indication on the scale of the score not being adequate for the range of outcomes studied. Still, with quality

scores it may be fully acceptable to have a high number of patients with the maximal score for quality (i.e. ESS=0), whereas a high number on score for minimal quality will warrant further expansion of the scale. Floor and ceiling effects were defined as more than 15% of patients having lowest or highest possible ESS, respectively. For this purpose, the score frequencies were examined separately for the whole period of 24 hours. A positive rating is given for absence of floor and ceiling effects in at least 25% of the patients [14].

Interpretability

The definition of interpretability is the degree to which one can assign qualitative meaning to quantitative scores [33]. For this purpose, the subgroup analyses planned a priori were examination of ASA-score, gender, age and type of anaesthesia (general anaesthesia versus regional anaesthesia). Ear, nose and throat surgery was excluded from the type of anaesthesia subgroup. A positive rating is given when mean and SD scores are presented of at least four sub-groups, and MIC is defined [14].

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10. PAPER II

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ORIGINAL ARTICLE

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Postoperative quality and safety using Efficacy Safety Score (ESS) and a wireless patient monitoring system at the ward: A randomised controlled study

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Background: Postoperative pain, side-effects and time to mobilisation are indicators for the quality of postoperative recovery. The aim of this randomised controlled study was to investigate if efficacy safety score (ESS) combined with a wireless patient monitoring system would improve these clinical outcomes for patients at a general surgical ward.

Methods: The trial included 195 patients randomised to a standard care group (SC-Group) or intervention group (INT-Group) receiving continuous wireless monitoring of vital signs combined with ESS during the first 24 postoperative hours. The primary outcome was time to mobilisation. Secondary outcomes were average pain, doses of postoperative opioids, unscheduled interventions, side-effects, patient satisfaction and length of hospital stay (LOS).

Results: Mean time to postoperative mobilisation was 10.1 hours for patients in the INT-Group compared to 14.2 hours in the SC-Group; this corresponds to an adjusted hazard ratio of 1.54 (95% confidence interval 1.04-2.28). INT-Group patients received a higher dose of oral morphine equivalents; 26 mg vs 15 mg, $P < .001$; reported lower intensity of pain on a 0-10 scale; 2.1 vs 3.3, $P < .001$; and had higher patient satisfaction on a 5-point scale; 4.9 vs 4.3, $P < .001$. The LOS was similar between the groups; 71 hours in INT-Group vs 77 hours in SC-Group, $P = .58$. No serious side-effects were registered in INT-Group, whereas two were registered in SC-Group.

Conclusions: Introducing ESS as a decision tool combined with a wireless monitoring system resulted in less pain, increased satisfaction and more rapid mobilisation for patients in this study.

Trial Registration: clinicaltrials.gov Identifier: NCT03438578.

1 | INTRODUCTION

Judgement of quality of postoperative recovery has changed from single physiological variables to a broader assessment of patient outcome, for example, ability to drink, eat and mobilise.[1] To achieve this, adequate and safe treatment of acute postoperative pain is important.[2,3] Despite increased attention, postoperative pain is still undertreated.[4] A Dutch study showed that 30% of patients had moderate or severe postoperative pain at rest,[5] and in a Norwegian study, 38% reported a mean pain intensity ≥4 on an 11-point numeric scale.[6]

Opioids are still standard care for management of acute postoperative pain, but the risk of severe adverse events can limit optimal dosing for analgesia.[7] Although over-dosing of analgesics after non-complicated anaesthesia and surgery is rare, it still represents a major safety challenge.[8,9] In a post-anaesthesia care unit (PACU) there are staffing and monitoring available to ensure quality and safety of the treatment. After discharge to an ordinary ward, there is less available capacity for frequent patient observation.

Postoperative patient side-effects, such as pain, nausea and vomiting, are often not documented in a standardised manner at the ward or put into a comprehensive overall evaluation or overview.[6,10] Early warning scores, such as the National Early Warning Score (NEWS), have been developed to standardise surveillance of vital functions,[11] but do not include patient's quality parameters. At the project hospital, NEWS was based on cumbersome registration using pen and paper.

Efficacy Safety Score (ESS) is a validated clinical decision tool for the first 24 postoperative hours including both the PACU and the ward periods.[12] It covers multiple components of patient safety and quality status while monitoring the patient's experiences of the quality of care, including pain at rest and at movement. The Patient Status Engine (PSE) from Isansys Lifecare Ltd. is a wireless, semiautomatic registration system of vital patient parameters from wearable medical sensors.[13]

The aim of this study was to test the hypothesis that quality of care could be improved by combining ESS and PSE during the ward period of the first 24 hours after surgery, with reduced time to mobilisation and improved pain management, while ensuring patient safety.

Editorial Comment

Despite improved postoperative pain treatment regimes on the hospital wards, variable and most often manual collection of routine clinical status of patients still poses a challenge. In this randomized clinical trial examing the post-operative period, introduction of an automated monitoring system enabled better pain relief, higher patient satisfaction, and slightly shorter post-operative hospital stay

2 | METHODS

2.1 | Design and setting

This single-centre, randomised controlled trial, with two parallel groups, was conducted at the Orkdal Department, St. Olavs Hospital, Trondheim University Hospital, Norway. Design and description of the study adhered to the Consolidated Standards of Reporting Clinical Trials statement (CONSORT).[14] The study was approved by the Regional Committee for Medical and Health Research Ethics (reference number 2017/1903/REK South East A) and registered at clinicaltrials.gov (NCT03438578).

2.2 | Eligible patients for the study

Eligible patients were identified from operating theatre lists of mixed surgery at a medium-sized surgical unit and recruited during pre-admission clinic or when prepared for surgery. Inclusion criteria were patients undergoing acute or elective surgery expected to be hospitalised more than 24 hours postoperatively. Exclusion criteria were patients <18 years of age, poor communication capabilities or when planned surgery was incompatible with mobilisation during the first 24 hours. All the patients were subjected to the same post-operative prescriptions and PACU discharge criteria, according to the hospital protocols.

The intervention and study observation period started when patients returned to the ward from the PACU.

The ward nurses obtained patients' written informed consent preoperatively and performed study enrolment. The patients were then randomly assigned to one of two groups—a standard care group (SC-Group) or an intervention group (INT-Group)—using a random number generator and sequentially numbered, opaque sealed envelopes set up a priori by the study personnel.[15] The ward nurses had to pick up the envelope at a restricted office after enrolment. Due to the clinically obvious monitoring system, neither the staff nor patients could be blinded to group allocation at the ward.

2.3 | Intervention group

In the INT-Group, the ward nurses assessed ESS in parallel with electronic automatic retrieved vital signs from the wireless monitoring platform PSE. The PSE is a class IIa CE-marked medical device (Isansys Lifecare Ltd.,) for hospital use monitoring heart rate, ECG, ventilation rate, axillar skin temperature, blood pressure and finger pulse oximetry; all from wireless and wearable sensors.[13] The PSE gives an updated NEWS every minute which is calculated from the sensors, except for blood pressure measurements which are initiated manually. Registration of ESS was recorded for storage on the bedside PSE device, done hourly during the first 4 hours after PACU discharge and then every second hour except when the patient was confirmed sleeping. In this study, we used bedside monitoring and visual warnings were displayed on the bedside device. Information on given medication was extracted manually from the patients' charts.

2.4 | Standard care group

In the SC-Group, NEWS was documented on paper formularies at least every 12 hours or with increased frequency in the presence of increased symptom severity. The hospital's clinical guidelines for ward postoperative pain assessment were to evaluate pain upon arrival, and then regularly and at least every 8 hours. For patients receiving continuous epidural—or peripheral nerve block analgesia—evaluation was to be done every 3 hours. Frequency of postoperative pain evaluation and notes about pain assessment and management

were registered together with given medication, extracted from the patients' charts.

2.5 | Ordinary postoperative protocol

Both groups followed the same protocols and indications for medication according to the hospital's clinical guidelines. At the study hospital, post-operative pain management is provided by prophylactic multimodal regular prescriptions according to instructions for the individual procedure: paracetamol, non-steroidal anti-inflammatory drugs, steroids, opioids, local anaesthesia in the wound, perineural blocks and regional anaesthesia. Extra medications beyond these are mainly intravenous or oral administration of oxycodone 2.5-5 mg. According to hospital guidelines, extra opioid medication may be administered when pain is >3 on an 11-point verbal numeric rating scale (VNRS) based on nurse judgement. Further, the guideline is to provide supplementary oxygen if saturation is <94% on pulse oximetry for patients not having chronic obstructive pulmonary disease and/or when needed as judged by the nurse.

2.6 | Outcomes

The primary endpoint of this study was time to full mobilisation, defined as being able to walk more than one step with or without support.[16] For both groups, mobilisation was attempted as early as possible after surgery, following the protocols for nursing plan and physiotherapy plan.

Secondary endpoints were average postoperative pain for the first 24 hours evaluated by an 11-point VNRS, milligrams of postoperative administered opioids, overall patient satisfaction on a 5-point scale, number of documented NEWS and pain assessments, presence of postoperative nausea and vomiting, unscheduled postoperative interventions, postoperative complications and length of hospital stay (LOS). For comparison of opioid medications, we used the conversion calculator for oral morphine milligram equivalents (MME) provided by the Norwegian Health Economics Administration (http://www.helfoweb.com/morfinekvivalenter/). Opioid additives to epidural anaesthesia are not part of this.

All the patients answered a questionnaire (see attachment) 24 hours postoperatively. This was performed by the study personnel and included questions about mobilisation, average pain, postoperative nausea and retching/vomiting, sleep, anxiety and worry, patient self-reported safety and security, mental function and satisfaction. We also registered unscheduled visits from physicians due to postoperative clinical issues or need for supplementary oxygen. Finally, we registered readmissions to the PACU or intensive care unit from the ward.

2.7 | Sample size calculations

A validation study addressing ESS in a total of 207 patients[12] was used for sample size calculations of the trial. A sample size of 130 patients (65 in each group) was required to show a 25% difference in mean time until full mobilisation from 12.6 (95% CI 10.6-14.6) hours with a power of 80% and an alpha level of 0.05 (Kane SP. SampleSizeCalculator. http://clincalc.com/Stats/SampleSize.aspx.). A sample size of 200 (100 in each group) included patients was considered sufficient to identify meaningful effect of the intervention on the primary outcome, allowing for some dropouts and missing data.

2.8 | Statistical methods

The Kaplan-Meier method and a log-rank test were used to analyse time to mobilisation, and group differences were analysed using the Mann-Whitney test. Additionally, Cox-regression was used to estimate hazard ratios for time to mobilisation between the intervention and control group, adjusting for age, American Society of Anesthesiologists (ASA) classification and sex. We used linear regression to estimate mean differences between the groups for opioid medication doses, numbers of pain assessments, NEWS performed and pain intensity assessments adjusting for age, ASA classification and sex. The precision of estimated effects is given by a 95% confidence interval. Categorical variables, such as reported oxygen therapy, postoperative nausea and retching/vomiting, were analysed using Chi-square tests. Patient satisfaction was analysed with Fischer's exact test based on a Chi-square test, due to low numbers of expected patients in some groups.

All collected data were registered in Microsoft® Excel® for PC, version 16. Data were analysed using SPSS version 25.0 (SPSS, Chicago, IL, USA).

3 | RESULTS

3.1 | Study groups

From 5 March 2018 to 18 October 2018, 201 patients were consecutively asked to participate; 200 were included and randomly assigned to two groups. As shown in the flow diagram (Figure 1), a total of 485 patients were potential candidates (ie planned in-hospital overnight stay and adequate communication skills) for the study. We were not able to attempt inclusion of all, due to limitations such as number of nurses and equipment available for study. Five patients were excluded, see Figure 1, resulting in data from 195 patients in the final analysis. Pre- and peroperative characteristics, length of stay and milligram equivalents of opioids given in the PACU, were similar between the groups (Table 1).

3.2 | Primary outcome

As the study progressed, it turned out to be a high number of prostatectomy patients (40 and 41 in the INT-Group and SC-Group respectively) who were instructed by the surgeon to not mobilise until the next day, making a cluster of mobilisation times for these patients in the data set within the 14-20 hour interval. After removing these radical prostatectomy patients from the analysis, the difference in mean time to mobilisation was 4.0 (95% CI 1.1-7.0) hours, with 10.1 (95% CI 8.1-12.2) hours for the INT-Group vs 14.2 (95% CI 12.0-16.3) hours for the SC-Group, $P = .008$.

The rate of mobilisation was 54% higher for INT-Group compared to SC-Group at any given time-point studied, when adjusted for age, ASA classification and sex: Hazard ratio 1.54 (95% CI 1.04-2.28).

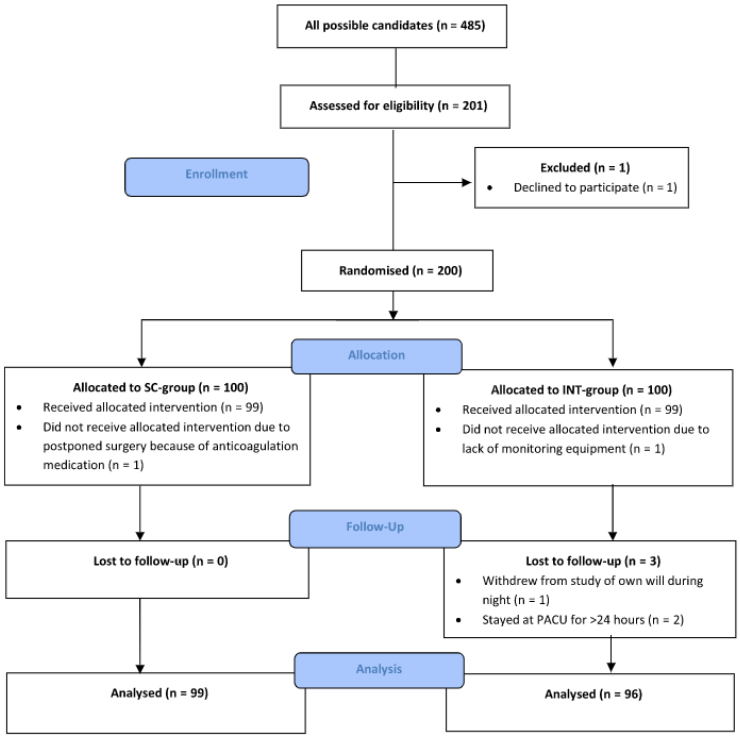

FIGURE 1 CONSORT 2010 flow diagram [Colour figure can be viewed at wileyonlinelibrary.com]

3.3 | Secondary outcomes

The difference in mean average intensity of pain on a 0-10 VNRS was 1.2 (95% CI 0.8-1.7), $P < .001$, with 2.1 (95% CI 1.8-2.9) for the INT-Group vs 3.3 (95% CI 2.9-3.7) for the SC-Group. The distribution of average pain is shown in Figure 2. An average pain intensity ≥4 on 0-10 VNRS was reported for 16% of the patients in the INT-Group and for 43% in the SC-Group.

The difference in mean opioid dose in MME provided at the ward was 10.3 (95% CI 4.2-16.4) mg, $P = .001$, with 25.5 (95% CI 20.9-30.0) mg in the INT-Group compared to 15.2 (95% CI 11.1-19.3) mg in the SC-Group. The distribution range is shown in Table 2. Figure 3 shows the relation of mean administered MME at the ward and average pain.

The difference in mean reported patient satisfaction on a 1-5 scale was 0.6 (95% CI 0.39-0.79), $P < .001$, with 4.9 (95% CI 4.9-5.0) for the INT-Group compared to 4.3 (95% CI 4.2-4.5) for the SC-Group. See Table 3 for distribution.

The difference in mean number of documented evaluations of pain was 5.3 (95% CI 4.7-5.9), $P < .001$, with 6.7 (95% 6.1-7.29) times for the INT-Group vs 1.4 (95% 1.1-1.6) times for the SC-Group. For 17 patients in the SC-Group, there was no documentation about pain for the study period.

Mean number of performed NEWS differed by 4.8 (95% CI 4.0-5.5), $P < .001$, with 8.2 (95% CI 7.4-9.0) in the INT-Group compared to 3.4 (95% CI 3.1-3.6) in the SC-Group.

Postoperative nausea and retching/vomiting were reported for 41 and 12 patients in the INT-Group, respectively, vs 45 and 21 patients in the SC-Group. This results in differences in proportions of 5.2% (95% CI −8.9-19.0), $P = .48$, and 9.3% (95% CI −2.0-20.5), $P = .10$, for nausea and retching/vomiting respectively.

Supplementary oxygen at the ward was provided to 57 patients in the INT-Group compared to 32 patients in the SC-Group, a difference in proportions of 25.6% (95% CI 11-59-38.25), $P < .001$.

Serious complications were not observed in INT-Group, but in two patients in SC-Group: One patient was accidentally found in a state of unconsciousness and seizure 6 hours after surgery. This happened again, and telemetrically ECG monitoring was established. An asystole alarm call went off, and the patient was treated for severe bradycardia at an intensive care unit. Another patient in the SC-Group was treated for having a stroke after mobilisation at the ward.

Minor complications were not reported in the SC-Group. Five patients in the INT-Group were identified by the nurses in need of extra treatment and follow-up: Two for pain treatment (nerve blocks established), two for treatment of hypotension and one for treatment of atrial fibrillation.

Mean LOS for the INT-Group was 70.9 (95% CI 63.1-78.7) hours compared to 76.6 (95% CI 61.0-92-3) hours for the SC-Group, a difference of 5.8 (95% CI −23.5 −12.0) hours, $P = .58$.

TABLE 1 Patient characteristics. Data are numbers or mean (± SD)

	INT-Group	SC-Group
Number of patients (n)	96	99
Age (years)	61 (±12.5)	62 (±13.3)
Height (m)	1.74 (±0.10)	1.71 (±0.10)
Weight (kg)	88.7 (±18.8)	84.2 (±19.0)
Body Mass Index (kg/m2)	29.3 (±6.9)	28.2 (±6.1)
Sex (female/male)	36/60	37/62
Duration of anaesthesia (min)	177 (±42)	182 (±40)
American Society of Anesthesiologists Status (n)		
ASA I	1	2
ASA II	40	38
ASA III	52	56
ASA IV	3	3
Type of surgery performed (n)		
Urology		
Robot assisted radical prostatectomy (RARP)	40	41
Gastric surgery (n)		
Hemicolectomy laparoscopic/-open	9/3	4/3
Bariatric surgery (Gastric sleeve)	12	7
Stoma reversal	9	8
Laparoscopic small bowel resection/stoma	4	5
Total colectomy	1	2
Other (diagnostic laparotomy, acute cholecystectomy, proctectomy	1	4
Orthopaedic surgery (n)		
Shoulder joint replacement	10	11
Ankle arthrodesis	2	4
Hip-/knee joint replacement	2	2
Fracture fixation	3	5
Shoulder joint stabilisation/reconstruction	0	2
Type of anaesthesia performed (n)		
Gas anaesthesia: Propofol induction. Desflurane and fentanyl/remifentanil	59	60
Gas anaesthesia + Epidural Anaesthesia/Regional block	30	33
Spinal anaesthesia ± propofol sedation	7	6
Premedication (n)		
Paracetamol	96	99
Dexamethasone	93	98
Opioids	84	81
Non-steroidal inflammatory drugs	33	27
Fentanyl provided for surgery (mg)	0.25 (±0.11)	0.25 (±0.12)
Remifentanil provided for surgery (mg)	1.23 (±0.85)	1.27 (±0.89)
Morphine Milligram Equivalents provided at PACU (mg)	18.6 (±22.9)	18.0 (±21.5)
Time from end of surgery to discharge from PACU (min)	195 (±81)	201 (±80)

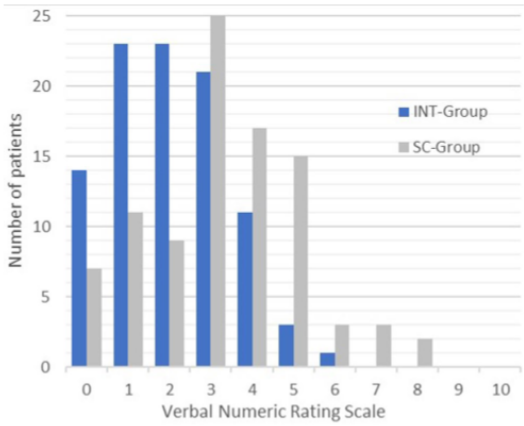

FIGURE 2 Distribution of patient-reported average pain for the first post-operative 24 hours on an 11-point verbal numeric rating scale (VNRS). Difference in mean average intensity of pain between the groups VNRS was 1.2, $P < .001$ [Colour figure can be viewed at wileyonlinelibrary.com]

4 | DISCUSSION

We report the results of the first randomised trial of postoperative use of the validated,[12] novel decision tool ESS integrated with wireless patient monitoring at a surgical ward. The results were earlier mobilisation, less pain, increased use of opioids and more satisfied patients during the ward part of the first 24 hours, by providing these clinical tools compared to standard care.

Mobilisation is a suggested golden goal for anaesthesia outcome because it encompasses the return of a spectre of physical capabilities.[1] Benefits from early mobilisation are shown for various types of postoperative patients.[17] In our study, it turned out that the prostatectomy patients got restrictions on early mobilisation. To avoid the results getting biased from this, we excluded these patients from the analysis for time to mobilisation.

Our data on pain may be compared with a previous Norwegian study, the mean intensity of postoperative pain was then 3.0 on an 11-point numeric scale during the first 24 hours, and 38% of the patients reported a mean intensity of pain ≥4.[6] Compared to this, our results are better for the INT-Group, whereas for the SC-Group they are similar. The same authors recommended that postoperative on-demand medication should be given if pain intensity is over 3 on an 11-point scale, which also was determined as a cut-off for moderate-to-severe pain.[18]

The reason for less pain in the INT-Group may both be more attention and more opioid medication. The nurses performed a higher number of NEWS and pain documentations in the INT-Group, and hence probably gave more attention to these patients. They also gave more opioids to patients in this group. This suggests improved communication and that the nurses were comfortable in giving a higher opioid medication.[7] The association between more opioids used and less subsequent pain is to be expected.

Not all patients in the INT-Group got opioids. The nurses identified those in need of more on an individual basis and provided these patients efficient on-demand pain relief, with maintained safety. Table 2 shows that some of these patients needed, and were given, far above-average opioid doses. The INT-Group was four times as likely to get opioid dosing within the three highest dose intervals. Extra opioids were given at lower VNRS score compared to patients in the SC-Group (Figure 3). The situation for the patients in the SC-Group with the highest average VNRS represents a major quality concern. More opioid treatment in the INT-Group did not result in any increase in emetic symptoms or respiratory problems. Further, potential more drowsiness from more opioids in the INT-Group was not shown. In fact, the opposite seemed to be the situation, as these patients had earlier mobilisation and a tendency of shorter hospital stay.

Our interpretation is that the frequent surveillance with the ESS tool made the nurses able to pick out and surveil those patients with an individual higher need of opioids, and to treat them accordingly with better pain results and no increase in side-effects.

All our patients got optimal non-opioid multimodal premedication analgesic regimes, but despite this, most needed opioid pain medication, as will be expected for major surgical procedures staying overnight.[19] Opioid analgesic is still a cornerstone in postoperative pain treatment and best controlled in the early phase in the PACU with titrated intravenous agents for reliable and rapid action.[20] Adequate early pain management may be associated with a lower incidence of persistent postoperative pain.[21] Early appropriate treatment with higher opioid dosages of short duration which maximises analgesia, while minimising the risk of later abuse, has been advocated.[22]

The pain assessment protocol in the INT-Group was more frequently scheduled and the documentation process itself was easier when compared to the hospital's standard protocol. This may explain some of the difference in the number of documented pain assessments.

The probability of receiving extra opioids for postoperative pain relief is significantly larger if a pain score is documented.[23] Absence of pain assessment and documentation were identified in a European survey report, which concluded with postoperative pain management being suboptimal.[24] The bedside documentation of ESS and automated NEWS by the PSE system is easier than manually performed NEWS, with subsequent documentation into patient

TABLE 2 Distribution range of total morphine milligram equivalents (MME) given at ward during the first 24 post-operative hours, n (per cent). Difference of mean provided MME between the groups was 10.3 mg, $P = .001$

	0 mg	1-19 mg	20-39 mg	40-59 mg	60-79 mg	>80 mg
INT-Group (n = 96)	12 (12.5%)	36 (37.5%)	24 (25.0%)	14 (14.6%)	8 (8.3%)	2 (2.1%)
SC-Group (n = 99)	34 (34.4%)	37 (37.4%)	22 (22.2%)	3 (3.0%)	2 (2.0%)	1 (1.0%)

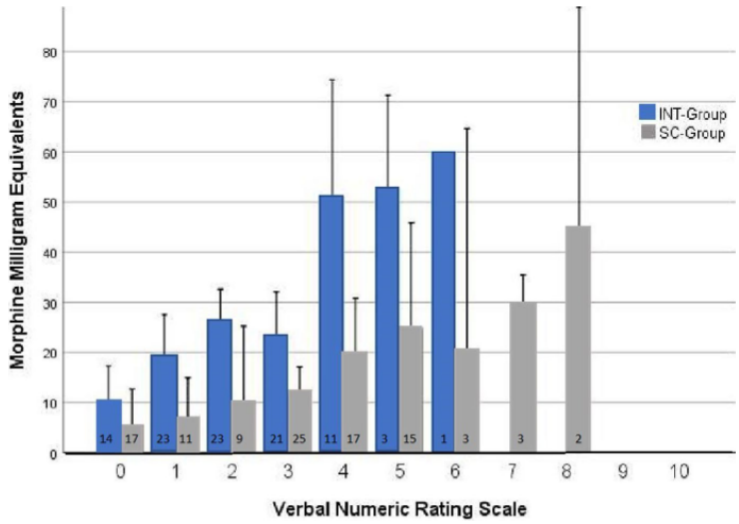

FIGURE 3 Mean distributed morphine milligram equivalents (MME) at the ward related to average pain on an 11-point verbal numeric rating scale (VNRS) (95% CI). Number of patients in respective columns. Differences between the groups were 10.3 mg for MME, $P = .001$, and 1.2 on the VNRS, $P < .001$ [Colour figure can be viewed at wileyonlinelibrary.com]

records at another location. The total lack of documentation on pain in the SC-Group for 17 of 99 patients is similar to earlier reports of no documentation in 9%-13%.[23,25]

It may be argued that simply enforcing the implementation of better pain and analgesia protocols may be as useful as the ESS + wireless monitoring system. Although this simple advice has been known for some time, documentation show that postoperative pain care has not improved to any major extent during the last years.[4-6] Also, if a better and more rigorously applied pain protocol results in individualised use of more opioid analgesics, it will be necessary to have protocols on monitoring safety and side-effects.[7-9] The ESS combined with wireless monitoring, as in our study, may be a way for systematic implementation of better overall care, including pain care.

The increased satisfaction in the INT-Group may be explained by improved pain relief, but other factors like being continuously monitored, regularity in follow-up and interactions with health care providers are probably also important. When patients become active participants in their own care it is shown that they become more comfortable and able to function.[26] However, the difference in satisfaction in our patients was mainly in the scaling of being 'satisfied' vs 'very satisfied', and this nuance may not be clinically significant outside a study setting.

Clinical outcomes are shown to be improved by the deployment of automated notification systems for vital signs monitoring in hospital wards.[27] The finding of increased use of oxygen therapy for the INT-Group reflects an expected effect of continuous monitoring. Patients in the INT-Group with hypotension and atrial fibrillation were identified by the monitoring system, and the call-out algorithm initiated by a high ESS was used. The same algorithm was used for the two patients given nerve blocks due to insufficient pain control. This contrasts the SC-Group patient who was accidentally found unconscious with seizures. We think this would have been discovered earlier with continuous monitoring. However, this study was not designed to have the power to make any conclusions about patient safety issues, but the case reports are noteworthy.

A strength of this study is that ESS is validated and easy to perform in daily clinical work. Also, we had two large and similar groups without major differences in baseline variables. The groups showed internal diversity in age, sex and surgery performed, but we chose this design with mixed patient characteristics to achieve good generalisability.

A weakness is that we did not test the two components of the intervention separately. We chose a pragmatic approach with a combination of two possible favourable interventions to maximise patient satisfaction and safety. Moreover, due to the monitoring system, neither the staff nor the patients could be blinded to group allocation. However, the possible influence from the study induced focus on post-operative care may have resulted in better care also in the SC-Group, with potentially better results than in everyday care.

The relatively restricted observation period is another limitation. Whereas the ESS is designed also to be used in the PACU,[12] we

TABLE 3 Overall patient satisfaction for first 24 post-operative hours on a 1-5 scale, n (per cent). The difference in mean between the groups was 0.6 (95% CI 0.39-0.79), $P < .001$

	1 Very dissatisfied	2 Dissatisfied	3 Neutral	4 Satisfied	5 Very satisfied
INT-Group, n = 89	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (6.7%)	83 (93.3%)
SC-Group, n = 90	2 (2.2%)	3 (3.3%)	6 (6.7%)	30 (33.3%)	49 (54.4%)

chose to have a totally similar non-ESS protocol for all patients in the PACU period, in order to tease out the true benefit during the first day on the ward. This is a period when the patients have pain, side-effects and need for frequent surveillance, more so than later in the postoperative course. Outcomes further on, for the next day and for clinical endpoints after discharge, will definitely be of interest, but were beyond the scope of this study.

Also, as the benefit of using ESS and wireless monitoring has been established, a further step will be to look at the time consume, nurse satisfaction and cost-benefit of using these methods in a daily routine, and also to look for potential simplifications in order to minimise the extra workload.

This study shows that important postoperative issues, such as pain and early mobilisation, were significantly improved with the use of the clinical tool ESS and PSE wireless monitoring at the ward.

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CONFLICT OF INTEREST

The authors have no conflict of interest. Isansys Lifecare Ltd. (UK) lent us the monitoring hardware and provided supplies at a reduced price.

AUTHOR CONTRIBUTIONS

E.S.: Study design, conduct, analysis and manuscript preparation. PCB, TILN, JR: Study design, analysis and manuscript preparation.

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11. PAPER III

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Clinical Study

Influence of a New "Call-Out Algorithm" for Management of Postoperative Pain and Its Side Effects on Length of Stay in Hospital: A Two-Centre Prospective Randomized Trial

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Background. We recently introduced the efficacy safety score (ESS) *as* a new "call-out algorithm" for management of postoperative pain and side effects. In this study, we report the influence of ESS recorded hourly during the first 8 hours after surgery on the mobility degree, postoperative nonsurgical complications, and length of hospital stay (LOS). *Methods*. We randomized 1152 surgical patients into three groups for postoperative observation: (1) ESS group ($n = 409$), (2) Verbal Numeric Rate Scale (VNRS) for pain group ($n = 417$), and (3) an ordinary qualitative observation (Control) group ($n = 326$). An ESS > 10 or VNRS > 4 at rest or a nurse's observation of pain or adverse reaction to analgesic treatment in the Control group served as a "call-out alarm" for an anaesthesiologist. *Results*. We found no significant differences in the mobility degree and number of postoperative nonsurgical complications between the groups. LOS was significantly shorter with 12.7 ± 6.3 days (mean ± SD) in the ESS group versus 14.2 ± 6.2 days in the Control group ($P < 0.001$). *Conclusion*. Postoperative ESS recording in combination with the possibility to call upon an anaesthesiologist when exceeding the threshold score might have contributed to the reductions of LOS in this two-centre study. This trial is registered with NCT02143128.

1. Introduction

The aim of modern management of postoperative pain is to enable functioning while relieving suffering; it is not enough to minimize side effects. Still, between 20% and 40% of surgical patients report high levels of postoperative pain, and almost 25% have experienced adverse effects of opioid analgesics [1]. Unsatisfying methods for evaluation of efficacy and side effects of analgesics, irregular recording of clinical information, and absence of a clearly defined "call-out algorithm" for nurses might contribute to a postoperative pain treatment suffering from both side effects and fatalities [1–5]. A large study performed in four New York hospitals revealed that patients with higher pain scores at

Table 1: Description of efficacy safety score (ESS).

	Score
Mental status	
Awake and alert patient	0
Awake patient but influenced by drugs; difficulties in communication	5
Acutely confused, upset/uneasy, hallucinated, or euphoric patient	10
Unresponsive patient	15*
Postoperative nausea and vomiting (PONV) status	
No postoperative nausea and vomiting	0
Postoperative nausea only	5
Postoperative nausea and vomiting/retching	10
Pain status at rest	
No postoperative pain	0
Low-intensity postoperative pain (VNRS 1–3)	1–3
Moderate-intensity postoperative pain (VNRS 4–6)	4–6
Severe-intensity postoperative pain (VNRS 7–10)	7–10
Pain status during mobilization	
No postoperative pain	0
Low-intensity postoperative pain (VNRS 1–3)	1–3
Moderate-intensity postoperative pain (VNRS 4–6)	4–6
Severe-intensity postoperative pain (VNRS 7–10)	7–10
General condition status	
Patient is stating feeling well	0
Patient has side effects apart from pain and nausea vomiting (e.g., sensation of warmth, flushing, itching, constipation, and urine retention)	5
Patient has acute severe circulation abnormalities (blood pressure ≤ 80 or ≥200 mmHg or mean arterial pressure < 50 mmHg and heart rate ≤ 40 or >110)	15*
Patient has developed acute severe respiratory abnormalities (unusual respiration or respiration rate < 9 or >20/min, long pauses in breathing, and shallow breathing)	15*

*Any single score of 15 (on either consciousness, circulation, or respiration) should call for immediate activation of acute assistance with the patient.

rest had significantly longer length of hospital stay (LOS) [6]. According to the latter investigators, moderate-to-severe pain at rest and reduced mobility after surgery were associated with increase neither in complications nor in morbidity and mortality postoperatively. The authors suggest that improved pain control might reduce LOS [6].

Other investigators recently reported that side effects of drugs had more than doubled in the hospitals that had introduced pain management guided by the patients' own numerical scale scores [7]. These authors suggested that more than just a one-dimensional numeric assessment of pain should be surveyed to make postoperative treatment safe and effective [7]. We developed the efficacy safety score (ESS), a new "call-out algorithm" for nurses in surgical departments, and implemented it in clinical practice at Kongsberg Community Hospital in Norway [8] after reports of fatalities due to postoperative overdoses of opioids in Norwegian hospitals [4, 5]. We established ESS after obtaining consensus in a DELPHI process between 10 international experts [9] on which parameters should be included in the score. The final version of ESS consists of the sum of two subjective parameters (Verbal Numeric Rating Scale at rest and during mobilization) and four vital parameters (consciousness levels, postoperative nausea/vomiting, circulation, and respiration status), as depicted in Table 1 [8]. The mathematical sum of ESS ≥ 10 is agreed upon by the experts as "the call-out alarm level" for informing the anaesthetist on duty, while any single score of 15 (on either consciousness, circulation, or respiration) is proposed as an alarm limit for immediate support of the patient [8]. Subsequently, we validated ESS for score criteria quality [10] and sensitivity for reflections of the patient's postoperative status [8]. Many factors like type of surgery, postoperative pain monitoring, and treatment can influence LOS [6], but, thus far, the topic has been undercommunicated. We hypothesized that better control of postoperative pain treatment and its side effects by monitoring ESS might influence the degree of mobility and morbidity in surgical patients and consequently reduce LOS. Thus, our aim was to validate the influence of recording ESS and the application of a "call-out algorithm" on LOS in two university hospitals in which the routine policy of registration of pain as "the fifth vital sign" had not been adopted yet. The primary endpoint of the study was to assess LOS in groups of patients with different types of clinical data records and "call-out

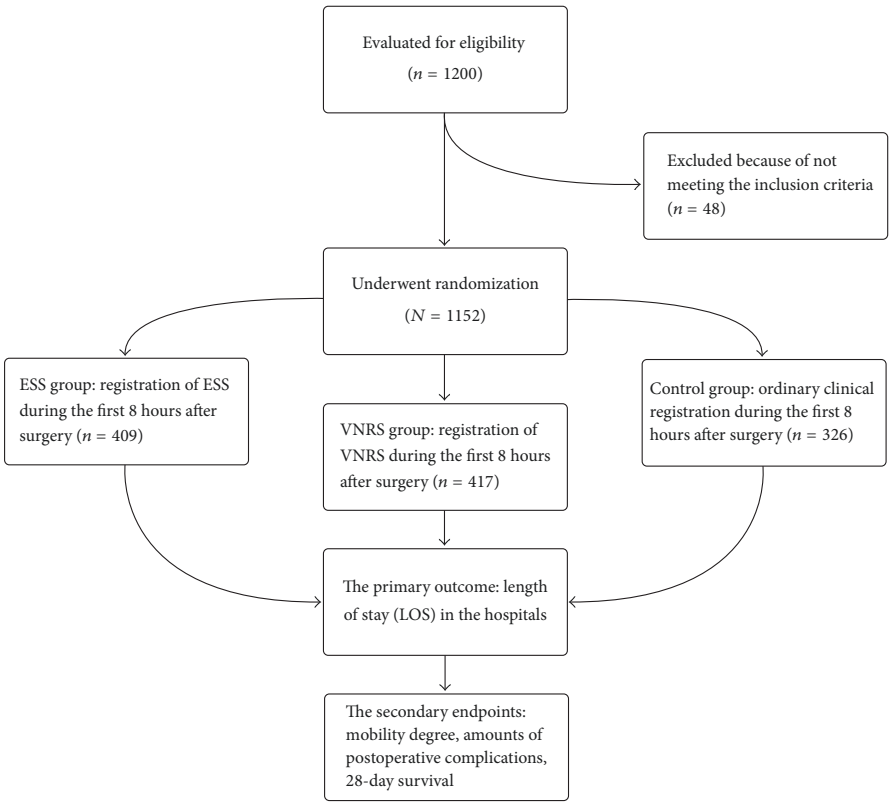

Figure 1: Flow chart of the study.

algorithms," while secondary endpoints were to compare the degree of mobilization, number of postoperative nonsurgical complications, and 28-day survival between the groups.

2. Methods

2.1. Ethics. Ethical approval of this clinical trial was provided by the Ethical Committee of Scientific Research Institute of Traumatology and Orthopaedics, Astana, Kazakhstan (ref. 2014-002, Chairperson: Professor T. Anashev), on 28 February 2014 and the Ethical Committee of Kuban State Medical University, Krasnodar, Russia (ref. 2014-027, Chairperson: Professor E. Bolotova) on 20 March 2014. In both countries, the study was considered as a quality assessment of efficacy and safety of pain treatment without any intervention apart from enforced surveillance. Thus, the project was approved with no need for informed consent of the patients.

2.2. Settings. The study was performed in the departments of abdominal surgery, orthopaedics, gynaecology, urology, and vascular surgery and high dependency units (HDU) at Astana University Hospital, Astana, Kazakhstan, and Krasnodar University Hospital, Krasnodar, Russia.

2.3. Inclusion Criteria. During the period from 1 March 2014 to 31 May 2015, all surgical patients whom we expected to need observation in hospital for more than 8 hours postoperatively and were able to communicate adequately with the nursing staff immediately after surgery were considered for inclusion.

2.4. Exclusion Criteria. We excluded patients below 18 years of age, patients with poor communication capabilities due to psychiatric diseases, dotage, and language problems, and patients who refused to communicate.

2.5. Procedures. Figure 1 depicts a detailed plan of the study. After inclusion, we randomized patients (by means of sealed envelopes) into one of three groups: (1) a record of ESS group (ESS group, Table 1), (2) a record of pain with Verbal Numeric Rate Scale group (VNRS group), in which 0 indicates no pain and 10 indicates "worst imaginable pain," and (3) a group in which ordinary clinical documentation was performed during the first 8 hours after surgery (Control group). In all groups, we recorded the mobility degree hourly during the first 8 hours postoperatively and noticed the degree of mobility from 0 to 3, where 0 indicates lack

of mobility, 1 indicates mobilization in bed, 2 indicates mobilization to a chair (bedside), and 3 indicates mobilization to standing. Table 1 presents detailed information about ESS with weighted scores. Based on the results of our study conducted at Kongsberg Community Hospital, Kongsberg, Norway, "call-out" alarm for ESS ≥ 10 was established for consultation by telephone or visit by the responsible anaesthesiologist or acute pain team on duty [8]. In the VNRS group, we based "call-out" decision on VNRS > 4 at rest, while in the Control group "call-out" decision was based on judgement of the patient's clinical condition by a nurse. We defined the ordinary evaluation by nurses in the Control group as the traditional routine clinical observation and care that were usually applied in these hospitals. Nurses in surgical departments and high dependency units recorded all clinical variables and mobility degree, while research fellows collected all demographic variables. The latter also registered all postoperative nonsurgical complications, such as cardiovascular (arrhythmias, ischaemic heart attacks, cardiac failure, low arterial blood pressure, and deep vein thrombosis) and pulmonary symptoms (atelectasis, pleural effusion, pneumonia, and pulmonary embolism) during the first 8 hours after surgery and contacted all patients or their relatives by mobile telephone for verification of 28-day survival. For evaluation of the physiological status of the patients, we used the American Society of Anaesthesiologists (ASA) Classification System. In that system, ASA I depicts a normal healthy patient, ASA II depicts a patient with mild systemic disease without substantial functional limitations, ASA III depicts a patient with one or more moderate-to-severe diseases and substantive functional limitations, ASA IV depicts a patient with severe systemic disease that is a constant threat to life, ASA V depicts a moribund patient who is not expected to survive without the operation, and ASA VI depicts a declared brain-dead patient whose organs are being removed for donor purposes.

2.6. Sample Size Calculation. We planned to recruit 180–200 patients into each group during a period of 12 months in each of the participating hospitals (total number: 1080–1200 patients) assuming an 18–20% difference in LOS between the groups for testing of sample size with 80% power and a two-sided significance level of 5%.

All subjective and objective clinical data were recorded in an especially designed program for mini iPad. Five mini iPads in each hospital were used for sampling and registration of clinical data that were subsequently transferred to the Structured Query Language (SQL) database using Clouds technology. Information about the record program with detailed video instructions is available on the following web site: http://essdb.no/index.php/en/application-en.

2.7. Statistical Analysis. Statistical data analyses were performed with cluster analyses of intracluster correlation coefficient, one-way ANOVA, and Chi square analyses using IBM® SPSS® Statistics 21.0. Data distribution was assessed using Shapiro-Wilk test. We used Kruskal-Wallis One-Way Analysis of Variance on Ranks to compare the difference between groups. If F value was greater than the critical value, ANOVA was followed by Dunn's method for pairwise multiple comparisons to obtain P values between groups. The data are presented as means ± standard deviations (SD) for age, Body Mass Index (BMI) as numbers and percentages (n, %) for the ESS values, gender, American Society of Anaesthesiologists (ASA) physical status classification, and type of surgery and anaesthesia. The results of hospital length of stay (LOS) in days are presented as median (solid line), mean (dashed line), and 10th, 25th, 75th, and 90th percentiles as vertical boxes with error bars; outliers are presented as open circles.

Additionally, we retested the "null hypothesis" by removing patients with extreme values of LOS from the data analysis. In this analysis, we defined patients with LOS below the 5th percentile and above the 95th percentile of the median as outliers and removed them from the LOS data of each hospital, the clustered LOS data of both hospitals, and the LOS data of all patients after laparoscopic cholecystectomy. Subsequently, we used the Kruskal-Wallis One-Way Analysis of Variance on Ranks to compare the difference between the groups. If F value was greater than the critical value, ANOVA was followed by Dunn's method for pairwise multiple comparisons to obtain P values between the groups. $P < 0.05$ was regarded as statistically significant.

3. Results

Totally, 1152 patients, 679 from the University Hospital of Astana and 473 from the University Hospital of Krasnodar, were included in the study during the period from 3 March 2014 to 26 May 2015. Tables 2 and 3 display basic demographic, anthropometric, and clinical characteristics of the three groups of patients studied in each of the hospitals. As depicted in Table 2, there were no statistically significant differences between the groups in demographic and clinical variables, such as age, BMI, gender, ASA classification, and type of anaesthesia and surgery in patients included in the study at the University Hospital of Astana. In contrast, we found significant differences between the groups in such clinical variables as ASA classification ($P < 0.0001$), type of surgery ($P = 0.0008$), and anaesthesia ($P = 0.0034$) at the University Hospital of Krasnodar. As shown in Table 3, 25.5% of the patients in the Control group were classified as ASA I versus 4.4% in the ESS group. Moreover, we listed 21.6% of the patients of the Control group as ASA III versus 39.7% in the ESS group. Concerning type of surgery, there were differences between the Control and the ESS groups in endocrine surgery (4.9% versus 16.0%) as well as in urological (15.6% versus 7.1%) and vascular (7.8% versus 2.7%) surgery, respectively (Table 3). In the Control group, more patients received spinal anaesthesia as compared with the ESS group (13.7% versus 3.8%). In the former group, more patients also were given total intravenous anaesthesia as compared to the ESS group (4.9% versus 1.6%). Finally, Table 3 also shows that general anaesthesia with sevoflurane and fentanyl was applied more often in the ESS group as compared with the Control group (55.2% versus 37.2%).

We observed no significant differences between the groups and hospitals concerning the degree of mobilization,

Table 2: Demographics, anthropometrics, and clinical characteristics of patients (n = 679) included in the study at the University Hospital of Astana.

	ESS (n = 228)	VNRS (n = 227)	Control (n = 224)	P value
Age: mean ± SD	43.4 ± 16.4	42.4 ± 16.4	44.9 ± 15.8	$P = 0.72^{*}$
BMI: mean ± SD	26.8 ± 6.1	26.3 ± 5.6	27 ± 5.9	$P = 0.39^{*}$
Gender				
Male: n (%)	116 (50.8%)	132 (58.1%)	120 (53.6%)	$P = 0.28^{**}$
Female: n (%)	112 (49.2%)	95 (41.9%)	104 (46.4%)	
ASA classification: n (%)				
ASA I	5 (2.2%)	6 (2.6%)	5 (2.2%)	
ASA II	145 (63.6%)	131 (57.7%)	126 (56.2%)	$P = 0.43^{**}$
ASA III	76 (33.3%)	89 (39.2%)	96 (42.9%)	
ASA IV	2 (0.9%)	1 (0.4%)	0	
Type of surgery: n (%)				
Orthopedic	202 (88.6%)	199 (87.6%)	207 (92.4%)	
Abdominal	10 (4.3%)	14 (6.2%)	9 (4%)	$P = 0.38^{**}$
Vascular	16 (7%)	14 (6.2%)	8 (3.6%)	
Type of anaesthesia: n (%)				
Sevo + fentanyl	74 (32.4%)	81 (35.7%)	79 (35.2%)	
Regional	38 (16.6%)	46 (20.2%)	45 (20%)	$P = 0.79^{**}$
SA ± EDA	102 (44.7%)/4 (1.7%)	93 (41%)/4 (1.8%)	89 (39.7%)/6 (2.6%)	
TIVA	14 (6.1%)	9 (3.9%)	8 (3.6%)	

*ANOVA; **Chi square analysis. Sevo: sevoflurane; EDA: epidural anaesthesia; SA: spinal anaesthesia; TIVA: total intravenous anaesthesia.

Table 3: Demographics, anthropometrics, and clinical characteristics of patients (n = 473) included in the study at the University Hospital of Krasnodar.

Variables	ESS (n = 181)	VNRS (n = 190)	Control (n = 102)	P value
Age: mean ± SD	55.2 ± 14.7	55.1 ± 15.6	56 ± 14.9	$P = 0.87^{*}$
BMI: mean ± SD	28 ± 17	27.8 ± 5.9	25.1 ± 4.5	$P = 0.08^{*}$
Gender				
Male: n (%)	69 (38.2%)	69 (36.4%)	49 (48%)	$P = 0.13^{**}$
Female: n (%)	112 (61.8%)	121 (63.6%)	53 (51.9%)	
ASA classification: n (%)				
ASA I	8 (4.4%)	11 (5.7%)	26 (25.5%)	
ASA II	99 (54.6%)	100 (52.6%)	53 (51.9%)	$P < 0.0001^{*}$
ASA III	72 (39.7%)	78 (41%)	22 (21.6%)	
ASA IV	2 (1.1%)	2 (1%)	1 (0.9%)	
Type of surgery: n (%)				
Abdominal	115 (63.5%)	125 (65.7%)	61 (59.8%)	
Endocrine	29 (16%)	18 (9.4%)	5 (4.9%)	
Gynaecology	19 (10.4%)	9 (4.7%)	12 (11.7%)	$P = 0.0008^{**}$
Urology	13 (7.1%)	18 (9.4%)	16 (15.6%)	
Vascular	5 (2.7%)	20 (10.5%)	8 (7.8%)	
Type of anaesthesia: n (%)				
Sevo + fentanyl	100 (55.2%)	103 (54.2%)	38 (37.2%)	
Sevo + fentanyl + EDA	77 (42.5%)	68 (35.7%)	45 (44.1%)	$P = 0.0034^{**}$
SA ± EDA	7 (3.8%)/6 (3.3%)	15 (7.8%)/7 (3.6%)	14 (13.7%)/4 (3.9%)	
TIVA	3 (1.6%)	2 (1%)	5 (4.9%)	

*ANOVA; **Chi square analysis. Sevo: sevoflurane; EDA: epidural anaesthesia; SA: spinal anaesthesia.; TIVA: total intravenous anaesthesia.

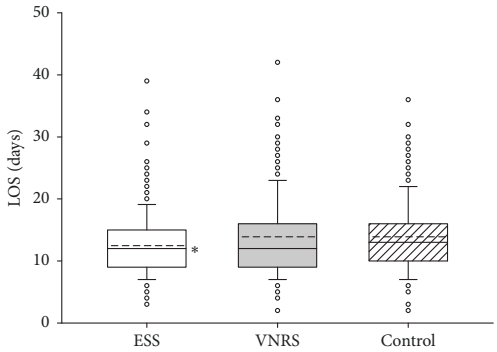

Figure 2: Length of hospital stay (LOS) of patients included in the study in University Hospital of Astana, Astana, Kazakhstan (n = 679). Data are presented as vertical boxes with median (solid line), mean (dashed line), and interquartile range with 10th percentile and 90th percentile error bars. Outliers are presented as open circles. $^{*}P = 0.011$ comparing ESS group versus Control group.

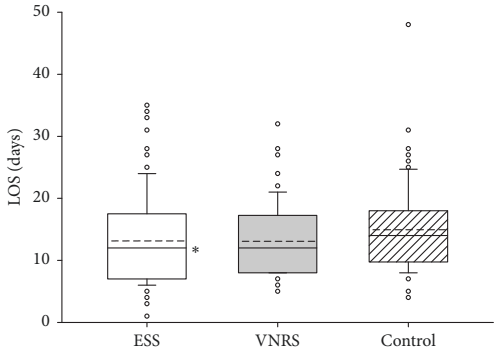

Figure 3: Length of hospital stay (LOS) of patients included in the study in University Hospital of Krasnodar, Krasnodar, Russia (n = 473). Data are presented as vertical boxes with median (solid line), mean (dashed line), and interquartile range with 10th percentile and 90th percentile error bars. In the VNRS group, the 10th percentile error bar is matching with the lower line of the box. Outliers are presented as open circles. $^{*}P = 0.022$ comparing ESS group versus Control group.

the number of postoperative nonsurgical complications, or mortality during the 28 days of observation time (data not presented). As depicted in Figures 2 and 3, in both hospitals, patients in the ESS group had significantly shorter LOS as compared to the Control group. Calculation of intracluster correlation coefficients revealed no significant differences in clustered data. Therefore, we pooled the results from both hospitals for further analyses of LOS which demonstrated a significant intergroup difference in LOS between 12.7 ± 6.3 days in the ESS group and 14.2±6.2 days in the Control group ($P < 0.001$) but not between the ESS and the VNRS group: 13.5 ± 6.2 days (Figure 4).

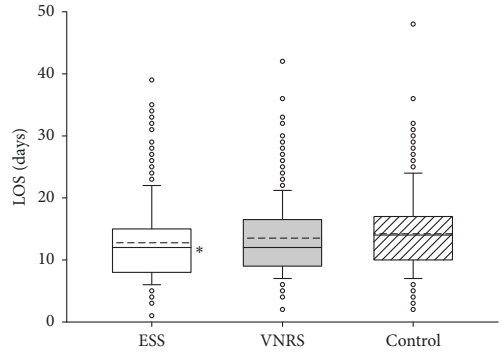

Figure 4: Length of hospital stay (LOS) of patients included in the study from both hospitals (n = 1152). Data are presented as vertical boxes with median (solid line), mean (dashed line), and interquartile range with 10th percentile and 90th percentile error bars. Outliers are presented as open circles. $^{*}P < 0.001$ comparing ESS group versus Control group.

In the ESS group, we found that 120 out of 409 patients (approximately 29%) were registered with ESS of more than 10 after the first postoperative hour, and therefore a telephone consultation or visit by the anaesthesiologist on duty was required according to the "call-out alarm" routine (ESS ≥ 10). However, the number of patients with ESS above 10 decreased gradually during the entire postoperative period, and, at 8 hours postoperatively, only 3.6% (n = 15) of the patients had ESS ≥ 10. In total, 517 visits were registered during the first 8 hours of observation in patients with ESS ≥ 10, whereas 4.4% (n = 23) were caused by "false alarms," according to the journal notes of the anaesthesiologists on duty. Correspondingly, in the VNRS and the Control groups, anaesthesiologist made 678 and 296 visits, respectively, whereas 4.7% (n = 32) and 2.3% (n = 7), respectively, were "false" according to the visiting anaesthesiologists.

In order to exclude the influence of different types of surgery, we carried out an analysis of a subgroup of 114 patients who underwent laparoscopic cholecystectomy. Table 4 displays the demographic and clinical characteristics of the patients. We did not find any significant differences between the three groups in such demographic or clinical characteristics as age (P = 0.15), gender (P = 0.61), or ASA classification (P = 0.39) (Table 4). Further, there were no differences between the groups in degree of mobility and number of postoperative nonsurgical complications (data not shown). However, as far as LOS after laparoscopic cholecystectomy is concerned (Figure 5), we observed significantly lower LOS in the ESS group versus the Control group (P = 0.003) and in the ESS group versus the VNRS group ($P <$ 0.001).

Record of ESS during the first 8 hours after laparoscopic cholecystectomy demonstrated that almost 30% (n = 11) of the patients (n = 36) had an ESS ≥ 10 at 1st postoperative hour, and according to the "call-out algorithm" they either had a telephone consultation or were seen by the anaesthesiologists

Table 4: Pooled demographics, anthropometrics, and clinical characteristics of patients included in the study after laparoscopic cholecystectomy from the university hospitals of Astana and Krasnodar ($n = 114$).

	ESS group ($n = 36$)	VNRS group ($n = 54$)	Control group ($n = 24$)	P value
Age: mean ± SD	51.8 ± 14.9	49.7 ± 13.4	56 ± 12.5	$P = 0.15^{*}$
BMI: mean ± SD	26.8 ± 4.2	29.2 ± 5.8	27.1 ± 4.5	$P = 0.06^{*}$
Gender				
Male: n (%)	10 (27.7%)	11 (20.4%)	5 (20.8%)	$P = 0.61^{**}$
Female: n (%)	26 (72.3%)	43 (79.6%)	19 (79.2%)	
ASA classification: n (%)				
ASA I	1 (2.7%)	4 (7.4%)	3 (12.5%)	
ASA II	23 (63.8%)	34 (62.9%)	11 (45.8%)	$P = 0.39^{**}$
ASA III	12 (33.3%)	16 (29.6%)	10 (41.6%)	
Type of anaesthesia: n (%)				
Sevo + Fentanyl	36 (100%)	47 (100%)	15 (100%)	

*ANOVA; **Chi square analysis. Sevo: sevoflurane.

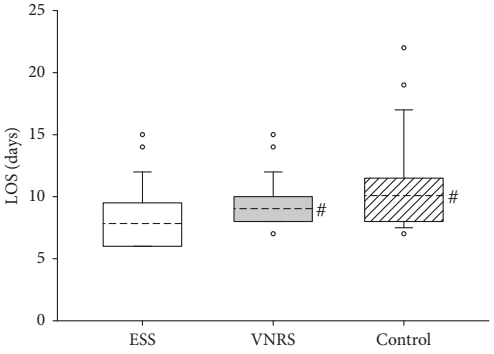

Figure 5: Length of hospital stay (LOS) of patients included in the study after laparoscopic cholecystectomy from both hospitals ($n = 114$). Data are presented as vertical boxes with mean (dashed line) and interquartile range with 10th percentile and 90th percentile error bars. In the ESS and VNRS groups, the 10th percentile error bar is matching with the lower lines of the boxes. Outliers are presented as open circles. $^{\#}$ESS group versus Control group, $P = 0.003$; $^{\#}$ESS group versus VNRS group, $P < 0.001$.

on duty. At the end of ESS registration 8 hrs postoperatively, only two patients had an ESS ≥ 10.

In the additional analysis of data from the University Hospital of Astana, we found totally 54 patients with LOS values below and above the 5% and 95% range of the median, respectively. These data were removed from their respective groups. Thus, we removed 19 patients from the ESS group, 15 patients from the VNRS group, and 20 patients from the Control group. Actually, the difference in LOS between the ESS and Control groups remained significant ($P = 0.003$ versus $P = 0.011$). Correspondingly, in LOS data collected at the University Hospital of Krasnodar, we omitted 10, 6, and 7 patients, respectively, from the ESS, VNRS, and Control groups. Intergroup comparison of LOS revealed that differences between the ESS and the Control groups remained significant ($P = 0.002$ versus $P = 0.022$) after omitting the patients with extreme values of LOS. After reanalysing the data, we also found a significantly lowered LOS in the VNRS group in comparison with the Control group ($P = 0.012$).

In the clustered data from both hospitals, we omitted 27, 36, and 28 patients, respectively, from the ESS, VNRS, and Control groups. The significant difference between the ESS and the Control groups ($P < 0.001$) was confirmed, and, additionally, we found a significant difference between the ESS and VNRS groups ($P = 0.011$). Finally, we also confirmed the significant difference between the ESS and the Control groups ($P = 0.003$) after omitting the patients with extreme values of LOS after laparoscopic cholecystectomy.

4. Discussion

The main finding of the present two-centre trial was that the length of stay in hospital was significantly lower in the ESS group as compared with the Control group, while we noticed no differences between the VNRS group and the Control group. Correspondingly, in both hospitals, subgroup of patients who underwent laparoscopic cholecystectomy had significantly shorter LOS in the ESS group as compared with the VNRS and the Control groups. Additional statistical analysis revealed that the differences between the ESS and the Control groups, separately in each hospital, and in the clustered data from both hospitals remained significant after omitting the patients with extreme values of LOS. The reanalysis of data also confirmed the significant difference between the ESS and the Control groups in patients after laparoscopic cholecystectomy.

A policy for routine medical record of pain, as "the fifth vital sign," has not yet been adopted by the University Hospital of Astana in Kazakhstan and University Hospital of Krasnodar in Russia. So far, the latter institutions make no routine use of any postoperative pain or quality assessment score, like the Numeric Rate Scale (NRS) or the Modified

Early Warning Score (MEWS), which have different objectives [11]. Consequently, there was no ethical problem for the medical staff of these institutions associated with the inclusion of patients into the Control group of the present study. Most advantageously, the trial was uninfluenced by any other pain score or "call-out algorithm" that could warn against emerging deterioration of patients' wellbeing or general condition. In order to improve the quality of the recorded data, we developed a special program for iPad with alarms that both reminded the nursing staff on the time of data acquisition and alerted the anaesthesiologists on duty in situations with ESS $\geq$ 10 or VNRS > 4 at rest. In order to avoid any bias, nurses not involved in the study collected the data in this trial. Actually, due to the simplicity in use and the popularity among the nursing staff, the administration of Kongsberg Hospital approved ESS as a method for assessment of efficacy and safety of pain treatment. Detailed information about ESS and the special program for registration on iPad is available on http://esscore.org/ and http://essdb.no/. We primarily tested ESS in a study that included 207 postoperative patients and validated the score against quality criteria proposed for measurement properties of health status questionnaires [10]. Retrospectively, we realize that the latter validation had several biases. Unfortunately, almost 97% of the patients received total intravenous and/or spinal/epidural/regional anaesthesia, and only 3% were anaesthetised with inhalational anaesthetics [8]. In contrast, in Krasnodar and Astana, most of the patients included were anaesthetised with sevoflurane and fentanyl. However, in spite of differences in type of anaesthesia and surgery, we found ESS $\geq$ 10 at 1st hour postoperatively in 29.3% of the patients. This was nearly the same percentage (29%), at the same time point, as in patients included in the validation study conducted at Kongsberg Hospital. This consistency is in agreement with a previously published clinical study [2] demonstrating that approximately 30% of all surgical patients suffered severe postoperative pain.

On average, pooled data from the two hospitals showed that LOS varied between 12 and 14 days in both hospitals. This is consistent with previously reported health data in Organisation for Economic Co-operation and Development (OECD) [12] demonstrating that the average LOS in Russia is approximately 13.6 days. However, according to European statistics published on the Internet [13], the average length of hospital stay for inpatients ranged from 5.5 days in Bulgaria to 9.6 days in Croatia, with Finland topping the list with an average LOS of 10.6 days. Today, LOS is often used as an indicator of hospital efficiency [13]. Nevertheless, too short average of LOS might cause negative effects on health outcomes [14]. A retrospective study representing three hospitals in Japan and two in the USA demonstrated that median LOS in hip fracture patients was 34 days in Japan and 5 days in the USA [14]. Meanwhile, survival rate at follow-up, six months after surgery, was 89.5% in Japan and 77.2% in USA. Moreover, a Cox regression analysis revealed that every 10-day increase in LOS after surgery was associated with a 26% reduction in the risk of mortality (hazard ratio = 0.744, P = 0.014) after adjusting for LOS before surgery, patients' basic characteristics, number of complications, and country. Based on these findings, the authors concluded that shorter LOS after surgery did not necessarily predict better survival rate [14]. The recently published EuroHOPE study that included 59 605 hip fracture patients across seven European countries demonstrated that Hungary had the lowest LOS (12.7 days) and the highest one-year mortality (mean: 39.7%), whereas Italy had the highest mean LOS (23.3 days) and the lowest one-year mortality rate (mean: 19.1%) [15]. Thereto, a cohort study from Sweden, which included 116 111 patients with hip fractures, reported that shorter LOS was associated with increased risk of death 30 days after discharge from hospital but only among patients with LOS 10 days or less [16]. In contrast to the Swedish findings, a cohort study from the USA, which included a total of 188 938 hip fracture patients and a LOS of 11–14 days, was associated with 32% increased odds of death 30 days after discharge, as compared with a LOS of 1 to 5 days (odds ratio: 1.32) [17]. Large differences in the perioperative and postoperative care of hip fracture patients between Japan, Europe, and USA might give the opposite results [17]. Therefore, caution should be exercised when comparing results of this kind of studies between countries with dissimilar health care systems [17].

Our study has several limitations. We found no differences between the three groups in degree of mobility, number of postoperative nonsurgical complications, and 28-day survival. Actually, these findings were not surprising as modern anaesthesia [18] and postoperative analgesia techniques [19] principally demonstrate low incidences of postoperative complications and, consequently, low postoperative morbidity and mortality. However, we were not able to confirm the hypotheses that better monitoring of postoperative pain treatment and its side effects by assessment of ESS could have positive influence on the degree of mobility and, consequently, on the morbidity in surgical patients. Thus, the mechanisms causing the reduction of LOS in the ESS groups remain unknown. Another limitation of our study is that we did not record the total time and dosage of anaesthesia during surgery, and it is unclear whether they were comparable across all participants. We noticed no significant differences between the groups with regard to demographic variables as age, BMI, gender, ASA classification, and type of anaesthesia in the hospital of Astana. In contrast, we found significant differences between the groups regarding ASA classification, type of surgery, and anaesthesia in the University Hospital of Krasnodar. Indeed, these differences might have influence on the length of stay in University Hospital of Krasnodar and, consequently, be considered as a limitation of the study. In order to avoid the effect of differences in ASA classification, type of surgery, and anaesthesia on LOS, we selected and analysed additional data from all patients operated with laparoscopic cholecystectomy in the two hospitals. We found that LOS after laparoscopic cholecystectomy was significantly shorter in the ESS group as compared with the Control group. As mobility degree and morbidity displayed no significant intergroup differences, we could not identify the precise mechanism that contributed to the reduction of LOS in the ESS group. The latter, together with a lack of blinding procedures, also can be considered as limitations of the study. However, it is important to stress that surgeons responsible

for the discharge of patients were neither involved in the study nor informed about the primary endpoint of the clinical trial. Thus, we do believe that the medical staffs were sufficiently blinded to exclude any personal influence on the results of the study. In turn, the long average LOS in these hospitals can be partly explained by the fact that, in ordinary clinical practice in Kazakhstan and Russia, patients usually are admitted to hospital 1–4 days prior to surgery for different types of routine investigations, such as blood analyses and preoperative examination by the anaesthesiologist. Taking this into account, "real" LOS in Astana and Krasnodar hospitals might be close to that in Finland with an average of 10.6 days [13].

Finally, we believe that the university hospitals in Krasnodar and Astana have a great potential for reduction of LOS by introduction of such measures as multimodal fast-track programs for surgery [20], day case surgery for laparoscopic cholecystectomy [21], and home health care and institutional long-term care for patients who require additional services [22]. We also hope that the results of our study will inspire the administrators of the hospitals to introduce postoperative quality assessment scores like VNRS, MEWS, or ESS in routine clinical practice.

5. Conclusions

Registration of ESS hourly during the first 8 hrs after surgery and the extra attention of the anaesthesiologist on duty might have contributed to the significant reduction of LOS in both hospitals in this two-centre study. Since mobility degree and morbidity were not different between the groups, we could not identify the exact mechanisms behind the reduction of LOS in the ESS group. Consequently, elucidation of the impact of ESS on the length of stay in hospital after various types of surgery will need further randomized controlled trials.

Disclosure

Some results of the clinical study were presented as a poster at the International Anesthesia Research Society (IARS) 2017 Annual Meeting and International Science Symposium, Washington, DC, USA. The poster is available at the following link: https://files.aievolution.com/ars1701/events/12432/1600_Kuklin_1576_0417_091824.pdf.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of the paper.

Authors' Contributions

Drs. Lisa Dybvik and Erlend Skraastad contributed equally to this study.

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12. APPENDICES

Appendix A. Translated version of the postoperative questionnaire for study 2.

Questionnaire for postoperative ward period

Patient project number: _____ Informed consent (mark): ☐

Type of surgery: _____ Date of surgery: _____

1. **Time for mobilisation (walk more than one step with/without support)** ___:___
2. **Can you give the strongest intensity of pain (0-10) after the operation?** _____
   - In which situation was this? _____
3. **Can you give average pain after the operation (0-10)?** _____
4. **Have you experienced nausea?** Yes/No
   - If yes, how much of the time:
     One time – some – half of the time– most of the time – constantly
5. **Have you experienced retching/vomiting?** Yes/No
6. **Can you say something about your night sleep after the operation?**
   - Amount: None – reduced – normal – increased – very increased
   - Quality: Normal – unease/bad dreams – unease/pain – unease/bad thoughts
7. **Can you say something about anxiety/worry before the operation?**
   - None – some – medium – much – very much
8. **Can you say something about anxiety/worry after the operation?**
   - None – some – medium – much – very much
9. **Can you say something about your feeling of safety and security after the operation?**
   - Safe/secure – somewhat safe/secure – neither –somewhat unsafe/unsecure – unsafe/unsecure
10. **Can you say something about your ability to remember, reason, make decisions and pay attention after the operation?**
    - Normal – slightly reduced – reduced – some reduced – greatly reduced
11. **Any other complaints or side-effects after the operation?**
12. **Can you give your overall satisfaction with the treatment given after the operation?**
    - Very unsatisfied – some dissatisfied – neutral – satisfied – very satisfied
13. **Any other comments?**

Appendix B. First round response of the Delphi process from study 1 A.

Alphabetical setup of the response from the expert panel in the first round in the consensus process. Question asked: "To make an assessment of a postoperative patient's condition, what clinical information do you want?"

- Able to drink
- Able to eat
- Age
- Anaesthesia performed
- Anxiety
- Arrhythmia
- Behaviour – normal/unnormal
- Blood gas analysis
- Blood pressure
- Bradycardia
- Capillary refill time
- Chronic pain
- Comorbidity
- Complications to anaesthesia
- Complications to surgery
- Consciousness
- Disease/illness causing surgery
- Diuresis
- Dyspnoea
- Earlier pain medication
- Earlier performed surgery
- Haemoglobin
- Heart rate
- High-risk patient
- High-risk surgery
- History of opioid use
- Hyperthermia
- Hypothermia
- Hypovolemia
- Inspection of punction site(s)
- Localisation of pain
- Medication given
- Mental status
- Mobilisation
- Muscle strength recovery if muscle relaxation used
- Nerve block(s)
- Open airway
- Oxygenation
- Pain at movement/coughing
- Pain at rest
- Pain relief
- Pain – localisation, type and intensity
- Pain Visual Analogue Scale/Numeric Rating Scale
- Peripheral temperature – warm, cold
- PONV
- PONV prophylaxis
- Preoperative risk of PONV
- Sex
- Shivering
- Side effects
- Skin turgor
- Surgery performed
- Sweating
- Tachycardia
- Temperature
- Thirst
- Ventilation - depth
- Ventilation - frequency
- Weight / BMI

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