Bachelor's thesis

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Norwegian University of Science and Technology
Faculty of Medicine and Health Sciences
Department of Neuromedicine and Movement Science

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The effects of aerobic training on walking capacity in stroke patients

Bachelor's thesis in Human Movement Science
Supervisor: Ronny Bergquist
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Kunnskap for en bedre verden

ABSTRACT (EN)

Introduction Stroke is a serious medical condition affecting >15 million people worldwide each year. Impaired walking function is a common functional limitation that can occur after stroke, and that can present major challenges for the patient in the performance of daily activities. The aim of this narrative review is to assess whether aerobic exercise can improve walking capacity in stroke patients. **Methods** The databases used to identify relevant studies were PubMed, SPORTDiscuss, Web of Science, Google Scholar, and MEDLINE. Walking capacity was measured by a 6 Minute Walk Test and aerobic exercise was compared to conventional physical therapy or other low intensity rehabilitation methods. The database search resulted in 9 relevant studies. **Results** Six of the studies concluded that aerobic exercise had a statistically significant positive effect on walking capacity. Three studies found no significant or meaningful difference between the groups. **Conclusions** Comparisons of the studies led to the conclusion that aerobic exercise, lasting more than 6 weeks, using walking as a method of training has a positive effect on walking capacity in stroke patients.

ABSTRAKT (NO)

Introduksjon Slag er en alvorlig medisinsk tilstand som rammer >15 millioner mennesker over hele verden hvert år. Nedsatt gangfunksjon er en vanlig funksjonsbegrensning som kan oppstå etter slag. Dette kan by på store utfordringer for pasienten i utførelsen av daglige aktiviteter. Målet med denne systematiske oversikten er å vurdere om aerob trening kan forbedre gangkapasiteten hos slagpasienter. **Metode** Databasene som ble brukt for å identifisere relevante studier var PubMed, SPORTDiscuss, Web of Science, Google Scholar og MEDLINE. Gangkapasiteten ble målt ved en 6-minutters gangtest og den aerobe treningen ble sammenlignet med konvensjonell fysioterapi eller andre typer rehabilitering med lav intensitet. Databasesøket resulterte i 9 relevante studier. **Resultater** Seks av studiene konkluderte med at aerob trening hadde en statistisk signifikant bedre effekt på gangkapasiteten. De resterende tre studiene fant ingen signifikant eller meningsfull forskjell mellom gruppene. **Konklusjon** Sammenlikning av studiene førte til en konklusjon om at aerob trening, med en varighet på mer enn 6 uker, med gange som treningsmetode har en positiv effekt på gangkapasitet hos slagpasienter.

Keywords: Stroke, 6 Minute Walk Test, aerobic exercise, walking capacity.

Introduction

Stroke is a serious, deadly, and debilitating medical condition affecting >15 million people worldwide each year(1). Stroke occurs when the blood supply to the brain is disrupted resulting in oxygen deprivation, leading to brain damage and often functional impairments. A stroke can be caused by a blood clot in an artery supplying blood to the brain, called ischemia. This is the most common type of stroke. It can also be caused by a cerebral hemorrhage when a burst vessel causes a blood leak into the brain (2). Stroke can affect both young and old people, but most strokes occur in people over 65 years (1). The risk of stroke increases significantly with age (2). It is estimated that the number of first-time stroke patients will increase as a result of the increase in the elderly population (1). Stroke is an acute event, and the disabilities that follows a stroke is something both the individual and their family is not prepared to deal with. This may result in an inability to work and a need for financial aid (3). Most stroke patients will experience different functional limitations and impairments after the stroke, and these will be different for each patient. 65% of stroke patients will regain functional independence one-year poststroke (4). Still, stroke is the major cause of adult disability.

Physical activity is recommended for all humans in all ages in the population. It reduces mortality and the risk of other diseases, improves physical fitness and the ability to engage in daily activities (5). One of the biggest underlying risk factors for stroke is physical inactivity, and it can contribute to causing or exacerbating functional limitations once a stroke has occurred. It can also increase the chance of recurrent stroke. Physical activity and training after a stroke will therefore be of great importance to complement into the patient rehabilitation and life in general (5).

A common consequence of stroke is impaired walking capacity. This can present major challenges for the patients in the performance of daily activities, which may affect their social life and quality of life (6). Walking recovery will often be a stroke patient´s top goal (7). Poorer walking capacity can be a result of muscle weakness, plegia, loss of coordination, subtle changes in the brain, and cognitive impairments (8). Reduction in cardiovascular fitness ,due to inactivity poststroke, can also lead to walking impairments (7).
Muscle weakness is the largest cause of disability after stroke. However, increasing strength does not consistently reduce disability - it does not always carryover directly to better walking (9). Previous studies indicates that task-specific rehabilitation is important to achieve a

meaningful impact on walking function for patients who are ambulatory post-stroke (5). Rehabilitation after stroke should be individually adapted to each patient to assure the best effects on functional outcome (7).

A common test to measure walking capacity is the 6 Minute Walk Test (6MWT). The guideline of this test was officially introduced by the American Thoracic Society in 2002. In this protocol the subject is instructed to cover the greatest distance possible in 6 minutes walking back and forth a length of 30.5 meters (10). The test has a strong test-retest reliability as well as construct validity in stroke patients (11).

Most stroke patients will regain the ability to walk. However, many of them will not restore their walking endurance, speed, or the ability to perform daily activities independently (7). The ability to walk independently is a prerequisite for most daily activities, from crossing a street in time before the red light, to avoid obstacles in the way. Previous research shows that only 7% of stroke patients discharged from rehabilitation after four months met the criteria for community walking, which included the ability to walk 500 meters continuously at a speed that would enable them to cross a road safely (7). The aim of this narrative review is to assess whether aerobic exercise can improve walking capacity in stroke patients.

Method

The databases searched to identify relevant studies were PubMed, SPORTDiscuss, Web of Science, Google Scholar and MEDLINE. The terms used in the search were “aerobic exercise”, “aerobic training”, “cardiovascular exercise”, “cardiovascular training”, “stroke”, “walking capacity” and “gait capacity”. The search was conducted in February 2022. Studies matching the following inclusion criteria were included: 1) a primary data analysis from either a matched or randomized controlled trial (RCT); 2) the patients were stroke survivors; 3) written in English or Norwegian; 4) a 6MWT was conducted at baseline and the end of the intervention period; 5) the intervention group performed aerobic exercise; 6) the control group performed conventional physical therapy, or other forms of low intensity rehabilitation. All age groups were included. Meta studies and systematic reviews found in the search were also read to identify studies previously missed in the database search. The initial search identified 14 studies in PubMed, 4 in SPORTDiscuss, 17 in Web of Science, 203 in Google Scholar and

14 in MEDLINE. After screening abstracts and full-texts, applying inclusion criteria and removing duplicates, we ended up with 9 original articles considered relevant for our review.

The results will be presented in text including the protocols of the selected studies and mean difference in the performance of the 6MWT. The risk of bias in the studies will be assessed. A table presenting group characteristics, performance in the 6MWT and the p-value of the interaction between groups will also be included.

Results

Globas et al. (12) studied the benefits of high intensity treadmill exercise. The study included 36 subjects, 18 assigned to each group. Subjects aged >60 years who were >6 months poststroke were included. The duration of the intervention period was 3 months. The intervention group trained 3*/week on a treadmill, aiming for 30-50 minutes at an intensity of 60-80% of heart rate reserve (HRR). The control group spent 1 hour 1-3*/week doing conventional physical therapy. The mean difference in the 6MWT between baseline and post-training testing was 57.5 meters in the intervention group and 4.0 meters in the control group.

Gordon et al. (13) studied the effect of aerobic exercise on functional status and quality of life. The study included 128 subjects, 64 assigned to each group. Subjects aged ≥40 years who were 6-24 months poststroke were included. The duration of the intervention period was 12 weeks. The intervention group walked up to 30 minutes 3*/week at a target heart rate of 60-85% of predicted maximum heart rate. The control group received 25 minutes of massage 3*/week. The mean difference in the 6MWT between baseline and post-training testing was 43.4 meters in the intervention group and 9.2 meters in the control group.

Hornby et al. (14) studied the efficacy of high intensity stepping training. The study included 32 subjects, 15 assigned to the intervention group and 17 assigned to the control group. Subjects 1-6 months poststroke were included. There were no age requirements. The duration of the intervention period was 10 weeks which equaled 40 training sessions for both groups. The intervention group performed four 10-minute blocks of various stepping tasks, including speed and skill dependent treadmill training, overground walking and stair climbing at an intensity of 70-80% of HRR. The control group did tasks consistent with conventional

physical therapy. The mean difference in the 6MWT between baseline and post-training testing was 116.0 meters in the intervention group and 29.0 meters in the control group.

Jin et al. (15) studied the efficacy of ergometer cycling training. The study included 128 subjects, 65 assigned to the intervention group and 63 assigned to the control group. Subjects between the age of 42-68 years who were >6 months poststroke were included. The duration of the intervention period was 12 weeks. The intervention group trained on a stationary bike for 40 minutes 5*/week at a target intensity of 50-70% of HRR. The control group did conventional physical therapy at a matched duration. The mean difference in the 6MWT between baseline and post-training testing was 6.5 meters in the intervention group and 0.6 meter in the control group.

Kuys et al. (16) studied the effects of high-intensity treadmill walking. The study included 30 subjects, 15 assigned to each group. Subjects who newly had recovered their walking ability were included. There were no age requirements. The duration of the intervention period was 6 weeks. The intervention group performed 30 minutes of treadmill walking 3*/week with an intensity of 40% progressing to 60% of HRR, and 1 hour with conventional physical therapy per day. The control group performed conventional physical therapy only. The mean difference in the 6MWT between baseline and post-training testing was 107.0 meters in the intervention group and 60.0 meters in the control group.

MacKay-Lyons et al. (17) studied the effects of body-weight-supported treadmill training. A Pneu-Weight unweighting system was used. The study included 50 subjects, 24 assigned to the intervention group and 26 to the control group. Subjects aged >18 years who were <1 month poststroke were included. The duration of the intervention period was 12 weeks. Both groups trained 60 minutes 5*/week the first 6 weeks of the intervention and 3*/week the remaining 6 weeks. Each session consisted of 30 minutes conventional physical therapy for both groups. The control group spent the remaining 30 minutes performing overground walking at self-selected speed and pregait activities, such as weight shifting and balance training. The intervention group performed 30 minutes of body-weight-supported treadmill training. The aim was to perform at an intensity of 60-75% of peak oxygen uptake for at least 20 minutes. Body-weight-support was gradually decreased. The mean difference in the 6MWT between baseline and post-training testing was 89.3 meters in the intervention group and 35.5 meters in the control group.

Macko et al. (18) studied the effects of treadmill exercise rehabilitation. The study included 61 subjects, 32 assigned to the intervention group and 29 assigned to the control group. Subjects aged >45 years who were >6 months poststroke were included. The intervention group performed treadmill training for 40 minutes 3*/week at a target intensity of 60-70% of HRR. The control group performed 35 minutes of stretching and 5 minutes of treadmill walking 3*/week. The mean difference in the 6MWT between baseline and post-training testing was 49.0 meters in the intervention group and 6.1 meters in the control group.

Tang et al. (19) studied the effects of ergometer cycling training. The study included 57 subjects. As the study recruited subjects between the years of 2003 to 2006, 18 pairs were matched and included in the data analysis after the collection of data. Subjects <3 months poststroke were included. There were no age requirements. The duration of the intervention period was 4 to 5 weeks. Both groups received individualized conventional physical therapy for 60-90 minutes 5*/week. In addition, ergometer cycle training was performed by the intervention group at a target duration of 30 minutes 3*/week at a rate of perceived exertion between 4 to 6 out of 10. The mean difference in the 6MWT between baseline and post-training testing was 127.0 meters in the intervention group and 89.6 meters in the control group.

Toledano-Zarhi et al. (20) studied the effects of an early aerobic rehabilitation program, defined as training that commenced 1-3 weeks poststroke. The study included 28 subjects, 14 were assigned to each group. Subjects aged <80 years were included. The duration of the intervention period was 6 weeks. The intervention group performed 35-55 minutes of aerobic training split between treadmill, hand-bike machine and ergometer cycling training at a target intensity of 50-70% of maximum heart rate 2*/week. The intervention group also performed 45-55 minutes of supervised strength, coordination, and flexibility training in combination with one of the aerobic training sessions. The control group based their exercise on a home-exercise booklet which was provided for both groups. The mean difference in the 6MWT between baseline and post-training testing was 53.3 meters in the intervention group and 24.9 meters in the control group.

Table 1: Group characteristics, performance in the 6MWT (measured in meters) and p-value of the interaction between groups. SD= standard deviation.

Author (year)	Group(n)	Gender (women/men)	Age (mean±SD)	Baseline (mean±SD)	Post-training (mean±SD)	Δ mean 6MWT	p-value
Globas (2012)	Intervention (18)	4/14	68.6±6.7	274.4±113.0	332.1±138.0	57.5	<0.001
	Control (18)	9/9	68.7±6.1	261.2±177.0	265±189.0	4.0	
Gordon (2013)	Intervention (64)	35/29	63.4±9.4	247.1±141.5	290.5±152.4	43.4	<0.001
	Control (64)	35/29	64.9±11.1	228.0±138.7	237.2±146.4	9.2	
Hornby (2015)	Intervention (15)	3/12	57.0±12.0	116.0±88.0	232.0±149.0	116.0	=0.001
	Control (17)	5/12	60.0±9.2	131.0±108.0	160.0±111.0	29.0	
Jin (2013)	Intervention (65)	19/46	57.6±6.6	212.5±64.2	219.0±64.3	6.5	<0.001
	Control (63)	18/45	56.3±6.5	212.4±51.1	213.0±51.7	0.6	
Kuys (2011)	Intervention (15)	8/7	63.0±14.0	177.0±130.0	284.0±147.0	107.0	=0.2
	Control (15)	10/5	72.0±17.0	219.0±147.0	279.0±163.0	60.0	
MacKay-Lyons (2013)	Intervention (24)	9/15	61.5±15.4	188.7±82.3	278.0±88.6	89.3	=0.015
	Control (26)	13/13	59.0±12.7	195.5±77.7	231.0±80.1	35.5	
Macko (2005)	Intervention (32)	10/22	63.0±10.0	232.0±22.2	281.0±24.0	49.0	=0.018
	Control (29)	8/21	64.0±8.0	258.5±33.2	264.6±30.5	6.1	
Tang (2009)	Intervention (18)	7/11	64.7±3.6	207.0±46.6	334.0±33.1	127.0	=0.23
	Control (18)	7/11	65.7±2.3	198.9±40.2	288.5±38.9	89.6	
Toledano-Zarhi (2011)	Intervention (14)	3/11	65.0±10.0	415.9±172.5	469.2±189.5	53.3	=0.06
	Control (14)	4/10	65.0±12.0	459.3±116.3	484.2±122.7	24.9	

All studies included in this review considered a p-value of <0.05 in the comparison between groups to be statistically significant, indicating that the training performed by the intervention group had a greater positive effect on performance in the 6MWT compared to the rehabilitation received by the control group.

Five of the studies conducted a power analysis before recruiting subjects to the study, of which four studies met their set criteria for number of subjects. Two studies conducted a power analysis after conducting the study to be used for further research. The remaining two studies did not perform such an analysis. Three studies were single blinded, two were double blinded, and one had a blinded assessor. Five studies analyzed their data based in the intention to treat protocol. Out of the four studies who did not report using this protocol, two had no missing data. One had missing data on one subject, but a secondary analysis showed no significant difference when excluding this subject in the primary analysis. One study had missing data and did not report how this affected their results. In four of the studies there was an imbalanced exposure to training.

Discussion

The aim of this narrative review was to assess whether aerobic exercise can improve walking capacity in patients after stroke. Nine studies were included. All studies had an intervention group performing aerobic exercise and used the 6MWT to measure walking capacity. Six of the studies concluded that aerobic exercise has a statistically significant positive effect on walking capacity as compared to conventional physical therapy or other forms of low intensity rehabilitation.

The studies by Tang et al. (19) and Toledano-Zarhi et al. (20) concluded that there was no significant difference between the groups. The study by Kuys et al. (16) had a significantly greater improvement in walking capacity compared to the control group. However, the confidence interval was wide, and the authors therefore concluded that there was no meaningful difference between the groups. The duration of the intervention period of these three studies were, respectively, 4-5 weeks, 6 weeks, and 6 weeks. The guidelines of the American College of Sports Medicine, as referred to by Globas et al. (12), states that a training period shorter than 6 weeks is probably insufficient, as the first adaptions to the

cardiovascular system are expected 2 to 6 weeks after the beginning of training. A common measurement of aerobic capacity is maximum oxygen uptake which can improve up to 20-50% after 2-6 months (21). A duration of more than 2 months would therefore be recommended. The short duration of the studies by Tang et al. (19), Toledano-Zarhi et al. (20) and Kuys et al. (16) may be one explanation to why they did not find a statistically significant or meaningful difference between the groups. Interestingly, these studies are three of the four studies who had an imbalance in exposure to training. An imbalance to exposure is considered to be a high risk of bias (22) favoring the group receiving more exposure. This may be a further proof of the importance of duration.

The studies by Toledano-Zarhi et al. (20), Tang et al. (19) and MacKay-Lyons et al. (17) enrolled subjects <3 months poststroke. A study conducted by Kwakkel et al. (23) concluded that at least 16% and up to 42% of improvements in function in the first 6-10 weeks poststroke can be considered spontaneous. Therefore, it is expected that some of the increase in performance in both groups can be attributed to spontaneous improvements. This may be another factor explaining why the studies by Toledano-Zarhi et al. (20) and Tang et al. (19) did not find a significant difference between the groups. Because the intervention period in the study by MacKay-Lyons et al. (17) exceeded these 10 weeks it can offer an explanation to why this study found a positive significant effect of aerobic training.

All studies included in this review had a target intensity and/or duration, which were not necessarily reached at the start of the intervention period. This is, especially in the studies with a duration ≤6 weeks, considered a weakness. In Kyus et al. (16) it took 2 weeks to reach the minimum intensity, which led to an intervention period with the desired intensity of 4 weeks.

A statistically significant effect does not necessarily equal a meaningful perceived change in walking capacity. Another study by Tang et al. (24) studied the relationship between the measured changes, using a 6MWT, and the perceived changes in walking after stroke. This study separated the subjects into two groups based on the performance in the baseline testing: a low baseline group (<288m) and a high baseline group (≥288m). The study concluded that an increase in performance in the 6MWT of 54.0 meters in the low baseline group, and 34.4 meters in the high baseline group, resulted in a significant perceived improvement in walking capacity. In the studies by Gordon et al. (13) and Macko et al. (18), there was a mean

difference in performance by the intervention groups of 43.4 meters and 49.0 meters, respectively. This could imply that the subjects did not perceive a meaningful change based on the conclusions by Tang et al. (24). In the study by Jin et al. (15) there is a mean difference in performance of 6.5 meters, leading to the conclusion that there was no meaningful perceived change. This study by Tang et al. (24) was the first to investigate these relations and the need for further studies is expressed.

Conventional physical therapy is a broad term that has been used in many of these studies. This may include strength training, balance and flexibility training and walking training adapted to the group or individual. It is often followed up by a physical therapist. Conventional physical therapy and amount of physical therapy also varies depending on how long it has been since the stroke, and the degree of impairments. Even though most of the studies use this term to define the training undergone by the control group, the methods and volume of training varies between studies. These variations make it difficult to compare the different types of aerobic training performed. The control group in the study by Gordon et al. (13) did not receive conventional physical therapy but rather massages. The control group in the study by Macko et al. (18) performed primarily stretching exercises and 5 minutes of walking which was defined as components of conventional physical therapy. It could be expected that the mean differences in the performance in the intervention and the control group in both studies would be more apparent compared to the rest of the studies where the control group performed more various training. However, as previously mentioned, the results by Gordon et al. (13) and Macko et al. (18) might indicate that the groups did not perceive a meaningful change in walking capacity although there was a significant difference in improved performance between groups.

A common limitation mentioned in all studies, but Hornby et al. (14) and MacKay-Lyons et al. (17), was the difficulty of generalization as the studies included relatively healthy subjects due to strict exclusion criteria. As a result, the subjects often had mild to moderate gait deficiencies and/or few other health related issues. For further research it may be relevant to study the effects of aerobic training on stroke patients with more severe impairments, including those who are non-ambulatory, and health related issues. This also raises the question on whether it is feasible and safe for a more affected group to perform a moderate- to high-intensity aerobic training program. Some of the studies in this review has inclusion criteria that targeted specific age groups. However, the mean age of all the studies is relatively

similar. All together the range in this review is wide covering all age groups. The total number of subjects in this review is 529, of which 207 are women. This relatively even distribution between gender and the wide range of age is positive in terms of generalization of this narrative review.

The training frequency varies from 3-5*/week between studies, except for Toledano-Zarhi et al. (20) where the subjects trained 2/*week. For both stroke patients and the general population, it is recommended that aerobic training should be performed 3-5*/week (21). Adaptions can occur with fewer training sessions and because of the short duration of the intervention period in the study by Toledano-Zarhi et al. (20) it is difficult to conclude whether the low frequency can serve as an explanation to the insignificant findings. The intensity and duration of the training sessions varied between the studies who concluded with a significant and meaningful improvement in walking capacity. There is also a variation in duration within some of the studies. Because different intensity measurements were used, it is difficult to make a direct comparison between the different intensities performed. Within each study there is also a broad range in the target intensities. However, all studies performed aerobic exercise at an intensity that can be considered moderate to high. Further research to discover the most optimal training program would be beneficial.

Most of our studies included walking as a method of training. This raises the question of whether it is the cardiovascular adaptions induced by the aerobic training that influences walking capacity, or if it is influenced by the practice of a specific task. As previously mentioned, task-specific training is important in rehabilitation with the aim of improving walking capacity. MacKay-Lyons et al. (17) and Macko et al. (18) both included walking in the protocol for the control group. It is likely that walking was included in the studies who defined the exercise performed by the control group as conventional physical therapy as well, since walking is a common component of conventional physical therapy. If both groups practiced walking, the differences in walking capacity explained by the importance of practice may be slightly reduced. However, there was still an imbalance in walking training, favoring the intervention groups using walking as a training method. Jin et al. (15) and Tang et al. (19) used ergometer cycling as the method of training in the intervention group, and Toledano-Zarhi et al. (20) used both regular and hand ergometer cycling. It is difficult to assess whether it was the method of training or the duration of the intervention, or a combination of both, that led to an insignificant finding in Tang et al. (19) and Toledano-Zarh et al. (20). The lack of

meaningful perceived performance in the study by Jin et al. (15) is likely to be explained by the use of ergometer cycling in the intervention. Based on these three studies it is not possible to conclude that ergometer cycling should be a part of a rehabilitation program with the aim of increasing walking capacity in stroke patients. It would be interesting to conduct further studies on this subjects as cycle ergometers have a low fall risk and is an accessible method of training present in most rehabilitation centers and gyms. Because of this low fall risk, ergometer cycling may be a feasible and safe method of training when conducting further research on aerobic training and gait capacity in a population with more severe deficits.

Based on the results of this narrative review it can be recommended for stroke patients to perform aerobic exercise, using walking as the method of training, when the aim is to improve walking capacity. The conclusions in this narrative review coincides with a Cochrane review conducted in 2016 (22), concluding that cardiovascular training is effective in increasing walking capacity, indicating that task specific training has a greater effect on walking capacity.

Conclusion

Nine RCT´s were identified in our literature search. Out of these studies, 6 concluded that aerobic exercise had a significantly greater effect on walking capacity compared to conventional physiotherapy or other low intensity rehabilitation methods. The remaining 3 found no significant difference between the groups. One of the studies who concluded with a statistical significance showed no practical meaningful improvement in the intervention group. Due to variation in protocols, it is not possible to make a conclusion on which intensity and frequency is the most optimal. Comparisons of the studies led to the conclusion that aerobic exercise, with a duration of more than 6 weeks, using walking as a method has a positive effect on walking capacity in stroke patients. Further studies should be conducted on patients with more severe health related problems.

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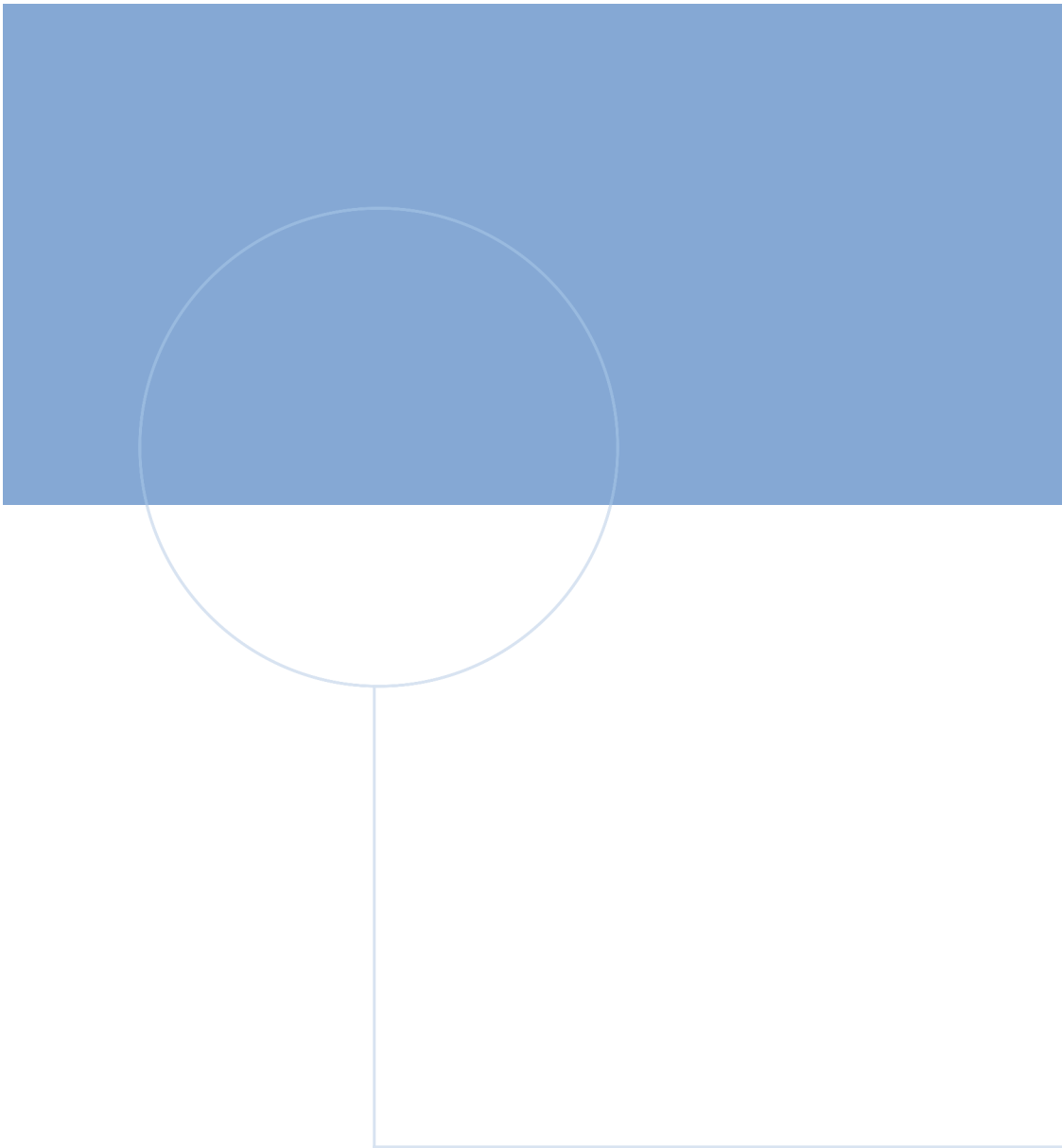

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