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Review Article: Systematic Review, Meta-Analysis, Integrative Review, Scoping Review

AEROBIC AND ANAEROBIC EXERCISE TO ENHANCE PHYSICAL FITNESS OF CHRONIC KIDNEY DISEASE PATIENTS ON HEMODIALYSIS: A LITERATURE REVIEW

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Abstract

Background: Chronic kidney disease is a condition where kidney has declining its function. It can cause a loss of physical capacity characterized by decreased body fitness, muscle strength and muscle endurance. Exercise programs to overcome the problem are still not common in dialysis clinics but there are several studies on exercise programs that have a positive effect on hemodialysis patients.

Objectives: This study aimed to review aerobic and anaerobic exercise to enhance physical fitness for chronic kidney disease patients on hemodialysis.

Design: The study design used was systematic review with using The Center for Review and Dissemination for writing guideline and the Joanna Briggs Institute Guideline for assessing the quality of summarized studies.

Data Sources: Search for articles accessed through database, such as ProQuest, Scopus, Science Direct, SAGE, and PubMed with keywords: Chronic kidney disease, aerobic exercise, anaerobic exercise, physical function and hemodialysis. The literature was published 2015-2021.

Review Methods: Joanna Briggs Institute Guidelines was used to assess the quality of the summarized studies. The presentation of the data will be done using descriptive techniques.

Results: The result of this systematic review shows that both aerobic and anaerobic exercise have a significant result for chronic kidney disease patient who undergo hemodialysis therapy. But aerobic exercise had a long-term impact for patients than anaerobic exercise. Combination of aerobic (ergometer cycle) and anaerobic exercise (resistance training exercise) also show a significant effect for physical fitness. The mechanism for enhancing physical fitness is done by strengthen the body muscle. The side effect of exercise is found minimum in most of study.

Conclusion: The combination of cycle ergometer exercise and resistance training exercise is one of the best exercises. The exercise could enhance the physical fitness by strengthen the muscle. The exercise could be done home based or intradialytic, but some articles state that intradialytic exercise is better than home based exercise.

Keywords: *Chronic Kidney Disease, Aerobic Exercise, Anaerobic Exercise, Physical Function, Hemodialysis.*

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INTRODUCTION

Chronic Kidney Disease (CKD) or CKD is a condition in which the kidneys are unable to maintain their function properly and irreversible damage occurs. CKD has some typical symptoms such as eGlomerulus Filtration Rate (eGFR) at least <60 ml/min for a period of <90, Creatinine Ratio (ACR) value> 30 mg/mmol and urine protein value> 50 mg/mmol (Lewis, 2012). According to the Third National Health and Examination Survey (NHANES III) it is estimated that the prevalence of chronic kidney disease in the United States in adulthood is 11% or 19.2 million of the population in the United States. Beside in Indonesia, the prevalence of chronic kidney disease at the age of 15 years (based on doctor's diagnosis) increased from 2.0%o (permile) to 3.8%o (permile) (Kementrian Kesehatan Republik Indonesia, 2018).

Chronic kidney disease (CKD) patient who undergo hemodialysis tend to experience decreasing their physical fitness because of the progressiveness of the disease and effect of hemodialysis itself. Physical fitness is the body's ability to carry out daily tasks and work vigorously without experiencing significant fatigue. Declining of kidney function causing loss in physical capacity as a result in physical inactivity which is characterized by decreasing physical fitness, muscle strength and muscle endurance (Huang et al., 2020). This physical inactivity also caused decreasing in physical function which characterized by disability and lead to mortality. Another symptom of decreasing physical function is derivation of oxygen uptake and muscle wasting. Hemodialysis therapy also have some side effect which could effect on physical function. Decreasing on metabolic system, like hypovolemia, changing in electrolytes and systemic inflammation caused by ultrafiltration lead to physical function derivation (Huang et al., 2020).

Based on the fact that CKD patient experience decreasing on physical function, exercise program needed to be set up. Several studies state that the level of physical activity in clients undergoing hemodialysis is in the range of 20%-50% lower (Chasani & Hidayati, 2017). Several studies on aerobic exercise indicated positive results on cardiovascular health. Anaerobic exercise is an intense physical activity with a short duration, driven by an energy source by muscle contraction and does not depend on the use of oxygen as an energy source (Riebe et al., 2018). Aerobic exercise is any activity that use large group of muscles that can be maintained continuously and rhythmic (Wahid et al., 2016). Aerobic exercise and anaerobic exercise are kind of exercise which suitable for CKD patients because it helps patient to enhance the muscle strength and cardiorespiratory system

The theme of aerobic and anaerobic exercise was choosen because based on research by (Scapini et al., 2019) explained that aerobic and anaerobic exercise were effective in increasing cardiorespiratory use in CKD patients undergoing hemodialysis. This study aimed to conduct a systematic review to assess the impact of aerobic and anaerobic exercise on physical function in CKD patients who undergo hemodialysis.

METHODS

Design

The study design used was systematic review. This study used Center for Review and Dissemination for writing guideline and Joanna Briggs Institute Guidelines for assessing the quality of summarized studies. Article selection is done by PRISMA checklist

Search Methods

Electronic database used to search the literature is ProQuest, Scopus, Science Direct, SAGE, dan PubMed. The articles are published around 2015-2021. To facilitate the searching, author uses keywords. The keywords use was "*chronic kidney disease" OR "chronic renal failure"," hemodialysis", "aerobic exercise" OR "aerobic training", "anaerobic exercise" OR "anaerobic training" OR "resistance training".* Inclusion criteria for this systematic review are (1) CKD patients who were in good

hemodynamic condition; undergo hemodialysis around ≥3 months (having hemodialysis frequency 2 times a week minimum); (2) 18-70 years old; (3) not having physical disability mainly on lower extremities; (4) study design used is RCT, quasi experimental, cluster randomized trial. Exclusion criteria for this systematic review are (1) patient with kidney transplant; (2) outcome criteria was not related to physical function

To get the final article, researcher did some step to screen it. After obtain some articles from database which identified by title, researcher would be identifying it by abstract. After identifying abstract, researcher screened the articles based on inclusion and exclusion criteria. The next step, researcher used JBI checklist to do critical appraisal. Final article then would be analyzed one by one and discuss it according to the specific aim of the study

Search Outcome

There are total 1.170 articles obtained from five database. From 1.170 articles which identified from the title, researcher found 920 articles. Some article doesn't match with researcher criteria (n=815) such as not quantify physical function parameter, systematic review type of article, using non- English language, the study for kidney transplant and peritoneal dialysis patient. There are total 105 articles after identifying the abstract and leaving articles as many as 45 after full text screening. The next steps are doing critical appraisal using JBI checklist for RCT and experimental study. And there are obtained about 25 articles at the end of the screening procedure.

The final selection articles would be presented in Table 1. The main outcomes of this study were aerobic and anaerobic exercise associated with increasing physical function of CKD patients who undergo hemodialysis.

Quality Appraisal

The quality of article is assessed by Joanna Briggs Instruments (JBI). The type of JBI instrument used was RCT and quasi experimental. This instrument contained some statement which could guide us to do critical appraisal. For every statement there are four types of answer (yes, no, unclear and not applicable). JBI for RCT research contain 13 question and for quasi experimental contain 9 question. The information about the articles consists of author, date and year for study, outcome measure, population, exercise type, study design, duration and intensity of intervention.

Data Abstraction

The article was reviewed by two investigators independently. Study which met the inclusion criteria then reviewed by two investigators. Disagreement of some topic will be solved by third investigators.

Data Analysis/ Synthesis

Twenty-five studies were selected to be reviewed. Some data which will be extracted are mean ± SD, sample size or the mean change of physical fitness at baseline and end point. Extracted data are presented in Table 1.

RESULTS

Studies Characteristic

According to the five databases used in article search, we finally find 25 articles that match with inclusion criteria. On Fig 1 show the selection process of article screening. Another information such as author name, year, study design, intervention type, duration will be shown in Table 1. Based on quality assessment, from the 25 studies all the articles met the criteria of critical appraisal (>50%). Twelve articles had quality score around 66-77%, 11 articles had quality score around 54-65%, 1 article had quality score around 78-89% and 1 article had quality score around >90%. From total of 25 articles, there were 10 articles investigated about aerobic exercise, 6 articles about anaerobic exercise and 9 about combination of aerobic and anaerobic exercise. Each type of exercise had their own criteria of frequency, time and intensity.

Description of Respondents

Total respondent for all studies were 1.476 people. The range of age for all studies was 18-90 years. The comparison of gender for 23 studies (2 studies did not show about gender data) was 56% men (n= 761) and 44% (n=592) women. The range of age for all studies was 18-90 years. The comparison gender for 23 studies (2 studies did not show about gender data) was 56% men (n= 761) and 44% (n=592) women. For the hemodialysis duration, based on 14 articles, there were 6 articles had mean of hemodialysis duration around 14-29 months, 3 articles around 30-45 months, 3 articles around 46-61 months and 3 articles around 78-93 months. For the etiology of CKD in respondent mostly because of hypertension and diabetes mellitus (DM).

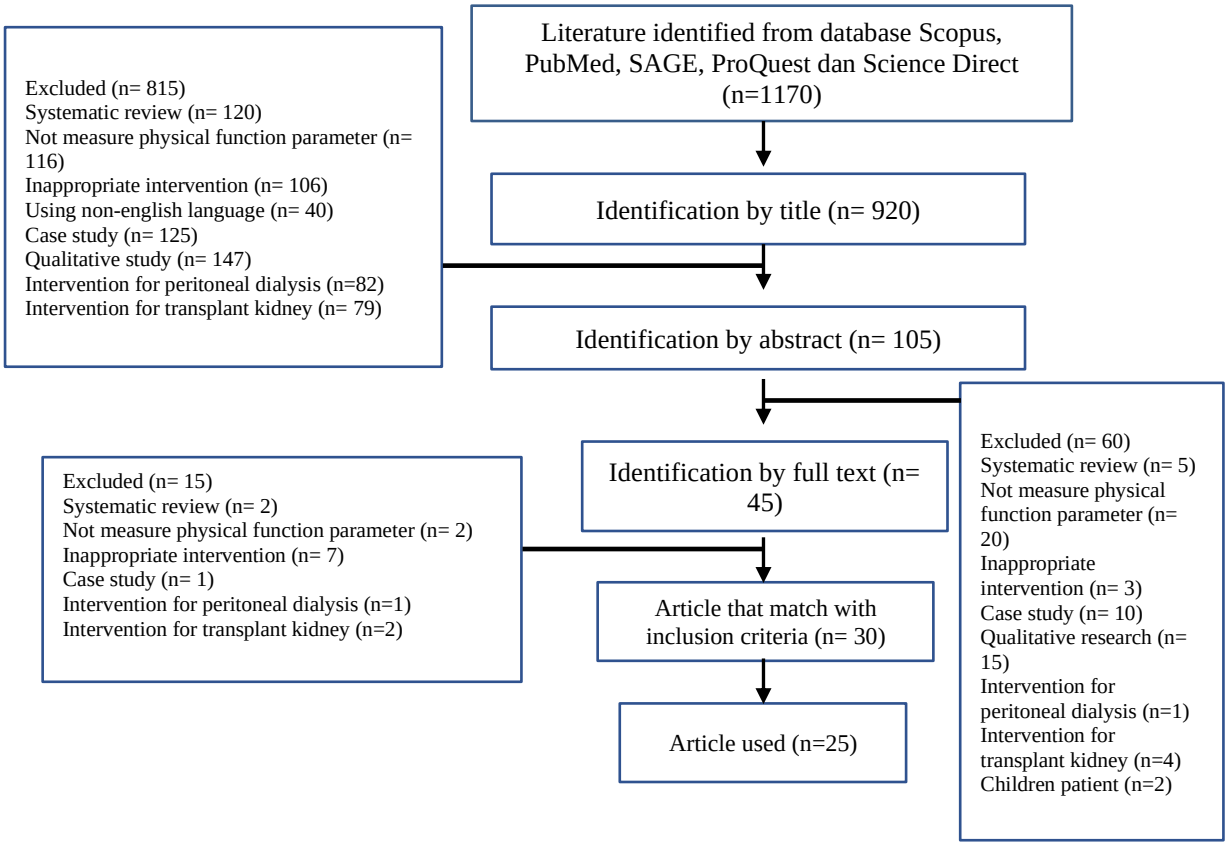

Figure 1. The PRISMA flow diagram is depicting the flow of information through the different phases of the systematic review.

Table 1. Summary of Included Article Aerobic and Anaerobic Exercise to Enhance Physical Fitness for Chronic Kidney Disease Patients on Hemodialysis.

Authors, years	Number of Subject	Study Design	Country (setting)	Intervention	Summary of Result	Time
(Nilsson et al., 2019)	11	RCT Pilot Trial	Norway	cycle ergometer	In the HIIT group, two of the three patients increased VO2peak by	16 weeks

Authors, years	Number of Subject	Study Design	Country (setting)	Intervention	Summary of Result	Time
					46% and 53%, respectively.	
(Bennett et al., 2016)	171	Stepped-wedge design of three group	Australia	Progressive resistance training	Exercise training led to significant improvements in physical function as measured by STS and TUG. (β = −1.59 P < 0.01) (β = 0.38, P < 0.01	12-36 weeks
(Frih et al., 2017)	41	RCT	Nephrology and Internal Medicine Service of CHU Monastir in Tunisia	Resistance and endurance training	Compared with control group, intervention group showed significant improvement in physical performance during the sit-to-stand-to-sit tests, handgrip force task, timed up and go test, and 6-min walk test	4 months
(Valenzuela et al., 2018)	67	RCT	Spain	Combination of endurance and resistance training	Exercise benefits were observed for 6MWT and STS-10 p < 0.01 And handgrip strength (p < 0.02)	14 weeks
(Fernandes et al., 2019)	39	RCT	renal unit in a quaternary hospital,	Ergometer cycle	A signifcant diference was observed in the six-minute walk test and lung capacity	8 weeks
(Andre de Casto et al., 2018)	43	prospective controlled study	Brazil	Resistance training program from moderate to	Patients presented significant improvements	3 years

Authors, years	Number of Subject	Study Design	Country (setting)	Intervention	Summary of Result	Time
				high intensity (3 times a week)	in MS (from 27.3 ± 11.58 Kgf to 34.8 ± 10.77 Kgf) and PWS (from 0.99 ± 0.29 m/s to 1.26 ± 0.22 m/s).	
(Bae et al., 2015)	10	Single group interventional study design	Outpatient HD unit in South Korea	Aerobic training using stationary bicycle	The six-minute walk test distance increased significantly after 12 weeks	12 weeks
(Rhee, Song, Hong, Choi, Jeon, Shin, et al., 2019)	22	non-randomized prospective trial	outpatient hemodialysis center at the Hallym University Kangdong Sacred Heart Hospital in Seoul, Republic of Korea	Aerobic exercise used ergometer cycle in 30 minutes. Then continued with exercise using elastic band (2-3 set; 10-15 repetition) in 5-10 minutes	After exercise completion, there were significant improvements in back muscle power, forward and backward trunk flexibility, vertical jump, elbow flexion, sit to stand test, and 6-minute walk test ($p < 0.05$).	6 months
(Cristina et al., 2019)	80	Pilot randomized clinical trial	Brazil	Resistance training with different intensity among the groups	After the training period, the HLG (High Load Group) increased lean leg mass compared with the CG. The HLG also displayed improvements in the pain and physical function domains	12 weeks

Authors, years	Number of Subject	Study Design	Country (setting)	Intervention	Summary of Result	Time
(Jamshidpour et al., 2020)	28	RCT	Dialysis Unit of Milad Hospital, Iran	combination of aerobic and anaerobic exercise	The 6MWT distance increased significantly in the exercise training group (36%). Bilateral hip flexor strength (right, 24.5%; left, 30.4%) (P > 0.05)	8 weeks
(Young et al., 2020)	64	RCT	UK East Midlands Renal Network	Cycling ergometer with intensity (RPE 12-14)	For tests of physical function; n=20 (39%) did not complete at least one test at baseline, n=33 (70%) at interim and n=30 (67%) at final	6 months
(Costa Rosa et al., 2018)	59	RCT	Haemodialysis Centre of the Bauru Hospital, Brazil	Strength muscle exercise with 15-20 repetition in 2 sets. Set and repetition will be increased. For each set, the training subjects performed repetitions until momentary failure occurred (maximum time 45-50 minutes)	Leg lean mass (p=0.04, effect size [ES] of 0.56), bone mineral content (p=0.02, ES of 0.65), leg strength in STT repetitions (p=0.01, ES of 0.66) and flexibility (p<0.001)	12 weeks

Anaerobic Exercise

Based of articles about anaerobic exercise, type of exercise mostly done was resistance training exercise. We found that this type of exercise had association with increasing on physical fitness of CKD patients who undergo hemodialysis. Research (Bennett et al., 2016) about anaerobic exercise program with a stepped wedge RCT design showed significant changes in the physical fitness test used (TUG,

30-STS) on baseline vs post intervention [(β = 0.38, P < 0.01) vs (β = −1.59, P < 0.01)]. Another article which aimed to compare high load and moderate load in resistance training exercise showed that intervention with high load intensity had a significant effect on physical fitness, leg lean mass, and QoL (Lopes et al., 2019). But in research of (Costa Rosa et al., 2018) which also compare of high load and moderate load intensity showed no significant effect in 6-MWT parameter of physical fitness but had significant effect on STS test.

Modification type of anaerobic exercise could be done by combine these two types of exercise (aerobic and anaerobic). For this type, we also found significant effect in physical fitness. Combination exercise done in home showed significant effect on gait speed and 10-STS test (Tao et al., 2015). The normal gait speed test indicated a significant between-group effect which means there is increasing scores for study group compared with control group [F (1.11) = 4.42, p = 0.038, h2 p 0:038]. The 10-STS test showed significant between-group differences [F (1.11) = 3.92, p = 0.050] with the greater scores in study group than in control group. Based on research (Ortega-Pérez de Villar et al., 2020) that combined between aerobic exercise (using cycle ergometer) and anaerobic exercise (using elastic bands) which compared intradialytic vs home based, showed a significant improvement in the physical fitness of chronic kidney disease patients on hemodialysis. Exercise which performed during dialysis was generally better than at home.

Aerobic Exercise

Based on several studies, it was stated that cycle ergometer is a definite aerobic exercise for CKD patients undergoing hemodialysis. We also found that aerobic exercise had significant effect in physical fitness. An article that examined the effects of aerobic exercise using a stationary bicycle for 30 minutes showed its effectiveness in increasing physical fitness. This is evidenced by the increase in the 6MWT test score at the post-intervention (419.00 ± 93.68 m) compared than pre-intervention (390.80 ± 78.62 m) (Bae, Lee and Jo, 2015). Another study on aerobic exercise used cycle ergometer stated that exercise with a cycle ergometer (high intensity) can improve the physical fitness of dialysis patients as evidenced by an increase in the 6-MWT value in the high intensity group compared to the moderate intensity group (466 [338–658] vs 403 [218–598]) (Nilsson et al., 2019).

The study that compared the cycle ergometer with the pedometer showed significant changes in the ergometer group and the pedometer group. The value of the SR test also increased in both groups (Bohm et al., 2014). Another type of aerobic exercise was walking exercise. The form of walking exercise also has a significant effect on physical fitness. It was proved by the increasing value of 6MWT and 10-STS in the intervention group compared to the control group [6-MWT: 328±96 m vs 367±113 m; P<0.001)] [10-STS: 20.5±6.0 sec vs 18,265.7 sec)] (Manfredini et al., 2017).

DISCUSSION

The physical effect of anaerobic exercise for the body is enhance the muscle strength. But increasing in muscle strength was not necessarily made the muscle function increase as well (Bennett et al., 2016). Another factor that improved muscle function was neuromuscular adaptation. Adaptations focused on increasing in skill acquisition through the nervous system and increased maximal muscle activation by way of motor unit synchronization, muscle recruitment, and increased neural activation (Hughes et al., 2018). The importance of the central neural component on strength adaptations is most evident when one limb is trained and the other limb goes untrained. In this situation, muscle CSA does not change in the untrained leg, yet a significant increase in strength occurs from training the contralateral limb (Hughes et al., 2018).

A significant increase in the value of gait speed was a good sign for hemodialysis patients in the context of maintaining physical fitness

and preventing worsening symptoms. It was because gait speed could predict future worsening conditions such as helplessness, hospitalization and mortality (Tao et al., 2015). Beside the gait speed one of physical fitness test was STS-10 which had the same effect of gait speed. Another study related to progressive resistance training exercise states that increasing STS test results are associated with increased lower extremity muscle strength. Another factor that causing significant different on gait speed and STS test was monitoring by health workers so that individuals could routinely carried out exercise programs. One of resistance training program targeted some upper and lower extremity like leg abduction, plantar flexion, dorsiflexion, straight-leg/bent-knee raise, knee extension and knee flexion) using elastic bands of various colors, where each color has a different color. different elastic strengths. Exercise was carried out in the first hour of hemodialysis. The frequency of exercise was 2 sets (with each set consisting of 15-20 repetitions) (Bennett et al., 2016). In some article the intensity of resistance training would be add in another week so that muscle could be trained harder till the limit of the patients.

Increasing in 6-MWT value on some articles reflected a positive change in the individual's cardiopulmonary capacity (Orcy RB et al, 2012 in Costa Rosa et al., 2018). The increasing in test trials had clinical relevance because physical fitness is a predictor of mortality in patients with chronic kidney disease (Roshanravan B, 2013 in Lopes et al., 2019). Improvements in post-exercise physical fitness were caused by increased protein synthesis, increased blood flow to the trained muscles and good adaptation of skeletal muscles in response to the training given to the patient (Lopes *et al.*, 2019). Besides, the physical exercise program could fight muscle atrophy, thereby reducing the incidence of muscle fatigue and helping to increase the patient's ADL activity.

One type of aerobic exercise was endurance training. Endurance training leads to adaptations in both the cardiovascular and musculoskeletal system (Brooks, 2011 in Hughes et al., 2018). Local adaptation in musculoskeletal was done by increasing in mitochondrial biogenesis and capillary density so that it could help body to distribute and using oxygen to produce energy. Beside, this mechanism could delayed the fatigue muscle (Joyner and Coyle, 2008 in Hughes et al., 2018). The form of HIIT exercise has also been shown to increase mitochondrial biogenesis by changing the frequency of exercise but the intensity remains the same (Granata et al. 2016b in Hughes et al., 2018). The proposed mechanisms for these improvements in endurance performance were improving neural function (maximal voluntary contraction, rate of force development [RFD]), increases in type IIA muscle fibers (less fatigable), and increased muscle–ECM–tendon stiffness (Hughes et al., 2018). A research also investigated that aerobic exercise could improve functional capacity of lung. The mechanism could be explained by increasing strength in type I muscles in the lower extremities that reflecting lung function. However, this hypothesis requires further research (Fernandes et al., 2019). Guidelines Of National Kidney Foundation (KDIGO, 2013), Exercise should be one of the pillars of therapy for adult patients undergoing hemodialysis with the aim of controlling cardiovascular risk factors (Lok et al., 2020). In another meta-analysis study, it was explained that an exercise period of 6 months was more effective than an exercise period of < 6 months. In addition, a combination strength exercise program with aerobic exercise is more effective than a single exercise (aerobic alone or strength exercise alone).

Combination exercise also good to enhanced physical fitness for CKD patients on HD program. On several study of combination exercise, 6MWT and 10-STS parameter increase significantly but not reach minimum score. It was because external factor from the participants, like low in motivation and adherence (Ortega-Pérez de Villar et al., 2020). Comparing about home-based exercise and

intradialytic exercise, research conducted by (Ortega-Pérez de Villar et al., 2020) also showed that intradialytic exercise was better than home-based exercise. Intradialytic exercise with combination program was proved could enhance the strength of back muscle power, elbow flexion test, sit-to-stand test, trunk flexibility test (forward and backward), vertical jump, dan 6-minute walk tes (Rhee, Song, Hong, Choi, Jeon, & Shin, 2019).

CONCLUSION

This systematic review had shown aerobic and anaerobic exercise need to be programmed for CKD patients who undergo hemodialysis. The intensity for each exercise need to be standardized based on existing guideline. Training for health workers to apply this kind of exercise also need to be prepared.

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DECLARATION OF CONFLICTING INTEREST

There is no conflict of interest for this study.

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AUTHOR CONTRIBUTION

Masita Widiyani: Contributing in prepare design, perform collecting article and analyzed the article.

Tintin Sukartini: Contributing for planning and supervised the work of systematic review.

Abu Bakar: Contributing in discussing for the result to the final manuscript.

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