

Supplementary File

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Summary of studies not included in meta-analysis

Arterial Resistance

Of 4 remaining studies (n=424) not eligible for meta-analysis, 1 non-randomized single group crossover study (n=22) of intradialytic resistance exercise for 13 weeks and 1 RCT of 26 weeks of intradialytic cycling (n=335) demonstrated no statistically significant difference in change in PWV or AI in the exercise group compared to the control group.^{1,2} Conversely, 1 RCT of 16 weeks of intradialytic cycling (n=32) showed a statistically significant decrease in PWV and AI in the exercise group compared to controls.³ One non-randomized study (n=35) showed a statistically significant reduction in PWV, but not AI with 12 weeks of intradialytic resistance exercise (Table 4).⁴

Blood Pressure

Studies not incorporated in the meta-analysis for BP effect included 1 RCT⁵ and 10 quasi-experimental studies (5 single group pre/post exercise studies^{1,6-9} and 5 non-randomized control group cohort studies).^{4,10-13} Two single group pre/post exercise studies demonstrated statistically significant reductions in 24 and 44 hour ambulatory SBP and DBP with 12 (n=18) and 13 week (n=19) intradialytic cycling interventions. One non-randomized cohort study (n=75) and one single group pre/post exercise study (n=18) demonstrated a small statistically significant decrease in predialysis diastolic BP, but no significant change in systolic BP after 26 weeks and 8 weeks of intradialytic cycling, respectively.^{7,13}

All 3 quasi-experimental studies that investigated the effect of intradialytic resistance training alone for 12 or 13 weeks on blood pressure demonstrated no statistically significant change in predialysis systolic or diastolic BP.^{1,4,14} In addition, 3 quasi-experimental studies

demonstrated no significant reduction in central or pre-dialysis systolic and diastolic peripheral BP after 12-26 weeks of intradialytic cycling.^{6,11,12} See Table 4.

Change in number of antihypertensive medications with intradialytic aerobic exercise was assessed in four studies.^{9,13,15,16} Of these, 1 single group pre-post intervention study of 26 weeks of intradialytic cycling (n=75) and one non-randomized control cohort study of 104 weeks of intradialytic cycling (n=80) demonstrated a statistically significant decrease in number of antihypertensive medications of -0.72 (no SD provided); p=0.02 and -0.55 (SD 0.06); p<0.001, respectively.^{13,15} In contrast, one single group pre-post study of 13 weeks of intradialytic cycling for 30 minutes thrice weekly (n=19) and one randomized cross-over study of 12 weeks of virtual reality aerobic exercise for 30 minutes thrice weekly (n=56) showed no significant change in the number of antihypertensive medications between intervention and control groups (mean difference -0.1 [SD 0.2; p>0.05] and 0 [SD not stated; p>0.05]).^{9,16} See Tables 2 and 4.

Myocardial Function

Of the remaining 2 studies that were not included in the meta-analysis, one compared a single group (n=24) before and after a 17-week intradialytic cycling intervention and demonstrated a 7.9% (SD 4.0) improvement in LVEF as measured by echocardiography following the intervention.⁶² A small single group study (n=23) with non-randomized cross-over design examined the effect of 12 weeks of low intensity intradialytic cycling on cardiac output and stroke volume, and demonstrated no significant difference between exercise and control periods in either outcome (Table 4).¹⁷

Myocardial Structure

A single small RCT of 13 weeks of intradialytic cycling demonstrated no statistically significant change in the proportion of individuals with severe left ventricular hypertrophy between intervention (n=20) and control (n=20) groups (Table 4).¹⁸

In 4 RCTs¹⁸⁻²¹ and a single group pre/post intervention study ranging from 12-44 weeks,⁶ no statistically significant difference was observed between intervention group and controls for LVEDV^{19,21}, LVSD^{6,18,20}, LVDD^{6,18,20} and LV posterior wall thickness (Table 4).^{6,20}

A statistically significant decrease of -11.1 g (95% CI:-15.8 to-6.4) in LVM measured by cardiac MRI was observed in an RCT of 130 individuals with intradialytic cycling for 30 minutes, thrice weekly over 26 weeks as compared to non-exercise controls.²¹ In contrast, no significant change in LVM measured using echocardiography was observed in a 17-week RCT of intradialytic cycling (n=15) as compared to 15 non-exercise controls (-9 g SD 8.2; p=0.2).²⁰

Cardiac Autonomic Dysfunction/Increased Sympathetic Activity

A single RCT (n=43) examined the effect of a combined resistance and aerobic exercise intervention for 30 weeks duration on outcomes of baroreflex sensitivity (BRS) and baroreflex effectiveness index (BEI). Within-group comparisons demonstrated a statistically significant increase in the exercise group's mean BRS from baseline to post-intervention ((6.1 SD 1.7 to 7.5 SD 1.8, p<0.05) but not in sedentary controls (baseline 5.5 SD 1.8; after 5.3 SD 1.6). BEI also increased by 11.7% (p<0.05) in the exercise group as compared to the control group which showed a small but insignificant reduction (-1.0%) in BRS (Table 4).²²

Table S1: Search strategy for each database

Database: Ovid MEDLINE(R) ALL <1946 to June 11, 2018>

Search Strategy:

- 1 exp Exercise/ or exp Exercise Therapy/ or exp Exercise Movement Techniques/ or exercise\$.ti. or exercise\$.ab. /freq=2 (282266)
- 2 (kinesiotherap\$ or (train\$ adj3 (physical\$ or anaerobic or aerobic\$ or resistance or strength\$ or muscle))).tw,kw. (27833)
- 3 or/1-2 (291128)
- 4 (intradialytic\$ or intra-dialytic\$ or extradialytic\$ or extra-dialytic\$.mp. (1669)
- 5 (((chronic\$ or progressive or diabetic) adj (kidney or renal or nephro\$ or glomerul\$)) or dialy\$ or h?emodia\$.mp. or ckd.tw. or esrd.tw. or ((diabet\$.mp. or Disease Progression/ or Recurrence/) and nephropath\$.mp.) or ur?emi\$.mp. or m?croalbuminuri\$.mp. or albuminuri\$.mp. or proteinuri\$.mp. or nephrosclerosis.mp. or glomerulosclerosis.mp. or glomerular sclerosis.mp. or *Glomerular Filtration Rate/ or (secondary adj2 hyperparathyroidism).mp. or ((tubulointerstitial or interstitial or renal or kidney) adj fibrosis).tw. or hyperphosphat?emia.tw. or vascular calcification\$.tw. or alport\$.mp. or denys-drash.mp. or glomerulopathy.tw. or hypoalbumin?emi\$.mp. or multicystic kidney\$.mp. or polycystic kidney\$.mp. or cystic kidney\$.mp. or calciphylaxis.mp. or tenckhoff.tw. or ((kidney or renal) adj (disease\$ or failur\$ or function\$ or insufficienc\$ or disorder\$ or dysfunction or replacement)).mp. or ((kidney or renal) and (ckf or crd or crf or eskd or eskf or esrf or hyperparathyroidism or end-stage or endstage or eGFR)).mp. or (((kidney or renal) adj

transplant\$) and (candidates or wait\$ list\$)).tw. or ((sclerosi\$ or fibrosi\$ or fibrotic).mp. and ((ureteral obstruction or nephritis or glomerulonephritis or nephrop\$).mp. or (obstruct\$ and (kidney\$ or renal or nephropathy)).tw.)) [High-Sensitivity Filter for Ovid Medline Chronic kidney disease] (571210)

6 (dialy\$ or h?emodia\$).mp. or ((end stage or endstage) adj (kidney or renal)).tw. or esrd.tw. or renal replacement.mp. or ur?emia.mp. or exp *Uremia/ or capd.tw. or h?emofilt\$.mp. or hyperphosphat?emia.tw. or ur?emic patient\$.tw. or secondary hyperparathyroidism.tw. or renal osteodystrophy.mp. or intradialy\$.tw. or *Hyperoxaluria/ or tenckhoff\$.tw. or autosomal dominant polycystic kidney.ti. or ccpd.tw. or ((exp *Renal Insufficiency, Chronic/ or ur?emic.tw. or hyperparathyroidism.mp.) and (renal or kidney or ckd).ti.) or (chronic.mp. and (ur?emi\$.mp. or *Kidney Diseases/)) or ((Severity of Illness Index/ or vascular.ti. or *Anemia/ or an?emi\$.ti. or nephrogenic.tw. or amyloid\$.mp. or rhabdomyolysis.mp.) and (exp Renal Insufficiency/ or *Kidney Diseases/)) or ((erythropoietin\$ or fistula\$ or acidosis).mp. and (exp Renal Insufficiency, Chronic/ or Renal Insufficiency/)) or ((Catheters, Indwelling/ or Catheterization,Central Venous/) and (exp Renal Insufficiency/ or heparin.mp.)) or (((kidney or renal) adj transplant\$) and (candidates or wait\$ list\$)).tw. or (encapsulating.tw. and scleros\$.mp.) [High-Sensitivity Filter for Ovid MEDLINE] (270432)

7 3 and (or/4-6) (3455)

8 limit 7 to "therapy (best balance of sensitivity and specificity)" (474)

9 clinical trial.mp. or clinical trial.pt. or random\$.mp. or tu.fs. or tu.xs. or th.fs. or control\$.mp. (9170364)

10 7 and 9 (2113)

11 (nonequivalent\$ or non equivalent\$ or pre\$1 or post\$1 or pretest\$ or posttest\$ or pre-test\$ or post-test\$ or pre-post\$ or quasi experiment\$ or quasiexperiment\$ or timeseries\$ or time series\$ or repeated measurement\$ or repeated series\$).tw,kw. (1151151)

12 (predialys\$ or postdialys\$ or preh?emodialy\$ or posth?emodialy\$ or preexercise\$ or postexercise\$ or pretrain\$ or posttrain\$ or preevent or postevent or preHD or postHD).tw,kw. (12358)

13 Comparative Study/ or (vs\$1 or vs or versus or compar\$).tw. (6077433)

14 or/11-13 (6798762)

15 7 and 14 (1457)

16 8 or 10 or 15 (2530)

17 limit 16 to "all adult (19 plus years)" (1556)

18 limit 16 to "all child (0 to 18 years)" (287)

19 16 not (18 not (17 and 18)) (2433)

20 (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or neonat\$).ti. (1230751)

21 19 not 20 (2401)

22 21 not (exp Animals/ not (Human/ and exp Animals/)) (2216)

23 (mice or rat or rats or cat\$1 or cattle\$1 or dog\$1 or goat\$1 or horse\$1 or rabbit\$1 or sheep\$1 or swine\$1 or pig\$1 or canine\$1 or feline\$1 or porcine\$ or calf).ti. (1673017)

24 22 not 23 (2189)

25 limit 24 to yr="1960 -Current" (2187)

2.

Database: Embase Classic+Embase <1947 to 2018 June 12>

Search Strategy:

- 1 exp *exercise/ or *exercise tolerance/ or exp *kinesiotherapy/ or exercise\$.ti. or exercise\$.ab. /freq=2 (264583)
- 2 (kinesiotherap\$ or (train\$ adj3 (physical\$ or anaerobic or aerobic\$ or resistance or strength\$ or muscle))).tw,kw. (38859)
- 3 or/1-2 (279480)
- 4 (intradialytic\$ or intra-dialytic\$ or extradialytic\$ or extra-dialytic\$).tw,kw. (2257)
- 5 (((chronic\$ or progressive or diabetic) adj (kidney or renal or nephro\$ or glomerul\$)) or ((kidney\$ or renal\$) adj disease) or (h?emodial\$ or peritoneal dialysis)).mp. or kidney failure/ or dialy\$.tw. or ((kidney or renal) adj (failur\$ or function\$ or insufficienc\$ or disorder\$ or dysfunction or replacement or damage)).tw. or exp *renal replacement therapy/ or (ckd or esrd or ur?emia).mp. or (diabet\$ and nephropath\$) (mp) or ur?emi\$.tw. or (nephrosclerosis or glomerulosclerosis or glomerular sclerosis).mp. or (hyperphosphat?emia or hyperuric?emia or hypoalbumin?emi\$).mp. or (secondary adj2 hyperparathyroidism).mp. or m?croalbuminuri\$.tw. or ((renal or kidney or vascular) adj calcification\$).mp. or exp *glomerulus filtration/ or ((tubulointerstitial or interstitial or renal or kidney) adj fibrosis).mp. or ((multicystic or polycystic or cystic) adj2 kidney).mp. or glomerulopathy.mp. or (alport\$ or denys-drash).mp. or *kidney dysfunction/ or ((kidney or renal) and (ckf or crd or crf or eskd or eskf or esrf or hyperparathyroidism or end-stage or endstage or eGFR)).mp. or (((kidney or renal) adj transplant\$) and (candidates or wait\$ list\$)).tw. or ((m?croalbuminuri\$ or albuminuri\$ or

proteinuri\$) and (diabet\$ or hypertension)).mp. [High-sensitivity Filter Ovid Embase Chronic Kidney Disease] (843618)

6 (h?emodia\$ or dialy\$).mp. or exp renal replacement therapy/ or ((end stage or endstage) adj (kidney or renal)).tw. or ur?emia.mp. or renal replacement.mp. or esrd.tw. or renal osteodystroph\$.mp. or autosomal dominant polycystic kidney.ti. or artificial kidney/ or renal hyperparathyroidism.tw. or ((*kidney failure/ or (chronic adj (kidney or renal)).tw. or *chronic kidney disease/ or ckd.tw.) and (erythropoietin.mp. or c reactive protein/ or calcification.mp. or vascular.ti. or hypertrophy.mp. or *hypertension/ or nephrogenic.mp. or stage.tw.)) or (((kidney or renal) adj transplant\$) and (candidates or wait\$ list\$)).tw. or ((indwelling catheter/ or exp vein catheterization/) and (exp kidney failure/ or heparin.mp.)) or ((ur?emic.tw. or hyperparathyroidism.mp.) and (kidney or renal or ckd).ti.) or (arteriovenous fistula/ and (catheter\$.mp. or nephrolog\$.tw.)) [High-Sensitivity Filter Ovid Embase Dialysis] (360985)

7 3 and (or/4-6) (4078)

8 limit 7 to "therapy (best balance of sensitivity and specificity)" (657)

9 random\$.tw. or placebo\$.mp. or double-blind\$.tw. or clinical trial\$.mp. or th.fs. or control\$.mp. (11285986)

10 7 and 9 (2373)

11 quasi experimental study/ or (nonequivalent\$ or non equivalent\$ or pre\$1 or post\$1 or pretest\$ or posttest\$ or pre-test\$ or post-test\$ or pre-post\$ or quasi experiment\$ or quasiexperiment\$ or timeseries\$ or time series\$ or repeated measurement\$ or repeated series\$).tw,kw. (1813540)

12 (predialys\$ or postdialys\$ or preh?emodialy\$ or posth?emodialy\$ or preexercise\$ or postexercise\$ or pretrain\$ or posttrain\$ or preevent or postevent or preHD or postHD).tw,kw.

(14804)

13 exp comparative study/ or (vs\$1 or vs or versus or compar\$).tw. (7697521)

14 or/11-13 (8776229)

15 7 and 14 (1837)

16 8 or 10 or 15 (2906)

17 limit 16 to (adult <18 to 64 years> or aged <65+ years>) (1409)

18 limit 16 to (embryo <first trimester> or infant <to one year> or child <unspecified age>)

(91)

19 16 not (18 not (17 and 18)) (2853)

20 (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or neonat\$).ti.

(1557914)

21 19 not 20 (2795)

22 21 not ((exp animal/ or nonhuman/) not exp human/) (2517)

23 (mice or rat or rats or cat\$1 or cattle\$1 or dog\$1 or goat\$1 or horse\$1 or rabbit\$1 or sheep\$1 or swine\$1 or pig\$1 or canine\$1 or feline\$1 or porcine\$ or calf).ti. (2033068)

24 22 not 23 (2493)

25 limit 24 to yr="1960 -Current" (2485)

3.

Search Strategy:

-
- 1 exp Exercise/ or exp Exercise Therapy/ or exp Exercise Movement Techniques/ or Exercise Tolerance/ or exercise\$.ti. or exercise\$.ab. /freq=2 (54898)
 - 2 (kinesiotherap\$ or (train\$ adj3 (physical\$ or anaerobic or aerobic\$ or resistance or strength\$ or muscle))).tw,kw. (14806)
 - 3 or/1-2 (59804)
 - 4 (intradialytic\$ or intra-dialytic\$ or extradialytic\$ or extra-dialytic\$).tw,kw. (469)
 - 5 exp renal dialysis/ or renal replacement therapy/ or exp Renal Insufficiency/ or exp Kidney Diseases/ or (renal\$ or kidney\$ or nephro\$ or glomerul\$ or nephri\$ or albuminuri\$ or proteinuria or anuria or ESRD or CKD or ESRF or uremia or uremic or prerenal\$ or pre-renal\$ or predialy\$ or pre-dialy\$ or pre-esrf or pre-esrd or hyperuremia or uraemia or dialy\$ or microdialy\$ or hemodial\$ or haemodial\$ or hemodiafiltrat\$ or hemofiltrat\$ or haemodiafiltrat\$ or haemofiltrat\$).tw. (58866)
 - 6 3 and (or/4-5) (907)
 - 7 (pediatr\$ or paediatr\$ or child\$ or adolescent\$ or infan\$ or newborn\$ or neonat\$).ti. (91879)
 - 8 6 not 7 (895)
 - 9 8 not (exp Animals/ not (Humans/ and exp Animals/)) (895)
 - 10 (mice or rat or rats or cat\$1 or cattle\$1 or dog\$1 or goat\$1 or horse\$1 or rabbit\$1 or sheep\$1 or swine\$1 or pig\$1 or canine\$1 or feline\$1 or porcine\$ or calf).ti. (3226)
 - 11 9 not 10 (894)
 - 12 limit 11 to yr="1960 -Current" (894)**

4.

Database: **SPORTDiscus**

#	Query	Results
S13	S11 AND S12	412
S12	(random* or (clinic* N3 trial) or control* or nonequivalent* or non equivalent* or pretest* or posttest* or pre-test* or post-test* or pre-post* or quasi experiment* or quasiexperiment* or timeseries* or time series* or repeated measurement* or repeated series* or predialys* or postdialys* or preh?emodialy* or posth?emodialy* or preexercise* or postexercise* or pretrain* or posttrain* or preevent or postevent or preHD or postHD or vs. or vs or versus or compar*)	300,118
S11	S10 NOT TI (pediatr* or paediatr* or child* or adolescent* or infan* or newborn* or neonat*)	883
S10	S9 NOT TI (mice or rat or rats or cat*1 or cattle*1 or dog*1 or goat*1 or horse*1 or rabbit*1 or sheep*1 or swine*1 or pig*1 or canine*1 or porcine*)	897
S9	S3 AND S8	1,013
S8	S4 OR S5 OR S6 OR S7	261,764
S7	TI (exercise* or kinesiotherap* or kinesio-therap*) or AB (exercise* or kinesiotherap* or kinesio-therap*)	122,574
S6	(train* N3 (physical* or anaerobic or aerobic* or resistance or strength* or muscle))	80,877

S5 DE "EXERCISE therapy" OR DE "EXERCISE therapy for children" OR DE "EXERCISE therapy for older people" OR DE "MENSENDIECK system" OR DE "ORTHOPTICS" OR DE "SWEDISH gymnastics" OR DE "THERAPEUTIC use of breathing exercises" 5,151

S4 DE "EXERCISE" OR DE "ABDOMINAL exercises" OR DE "AEROBIC exercises" OR DE "ANAEROBIC exercises" OR DE "AQUATIC exercises" OR DE "ARM exercises" OR DE "BACK exercises" OR DE "BREATHING exercises" OR DE "BREEMA" OR DE "BUTTOCKS exercises" OR DE "CALISTHENICS" OR DE "CHAIR exercises" OR DE "CHEST exercises" OR DE "CIRCUIT training" OR DE "COMPOUND exercises" OR DE "COOLDOWN" OR DE "DO-in" OR DE "EXERCISE adherence" OR DE "EXERCISE for children" OR DE "EXERCISE for girls" OR DE "EXERCISE for men" OR DE "EXERCISE for middle-aged persons" OR DE "EXERCISE for older people" OR DE "EXERCISE for people with disabilities" OR DE "EXERCISE for women" OR DE "EXERCISE for youth" OR DE "EXERCISE therapy" OR DE "EXERCISE video games" OR DE "FACIAL exercises" OR DE "FALUN gong exercises" OR DE "FOOT exercises" OR DE "GYMNASTICS" OR DE "HAND exercises" OR DE "HATHA yoga" OR DE "HIP exercises" OR DE "ISOKINETIC exercise" OR DE "ISOLATION exercises" OR DE "ISOMETRIC exercise" OR DE "ISOTONIC exercise" OR DE "KNEE exercises" OR DE "LEG exercises" OR DE "LIANGONG" OR DE "METABOLIC equivalent" OR DE "MULAN quan" OR DE "MUSCLE strength" OR DE "PILATES method" OR DE "PLYOMETRICS" OR DE "QI gong" OR DE "REDUCING exercises" OR DE "RUNNING" OR DE "RUNNING -- Social aspects" OR DE "SCHOOL exercises & recreations" OR DE "SEXUAL exercises" OR DE "SHOULDER exercises" OR DE "STRENGTH training"

OR DE "STRESS management exercises" OR DE "TAI chi" OR DE "TREADMILL exercise"

OR DE "WHEELCHAIR workouts" OR DE "YOGA" 153,536

S3 S1 OR S2 8,346

S2 TI (renal* or kidney* or nephro* or glomerul* or nephri* or albuminuri* or proteinuria or anuria or ESRD or CKD or ESRF or uremia or uremic or prerenal* or pre-renal* or predialy* or pre-dialy* or pre-esrf or pre-esrd or hyperuremia or uraemia or dialy* or microdialy* or hemodial* or haemodial* or hemodiafiltrat* or hemofiltrat* or haemodiafiltrat* or haemofiltrat*)

OR AB (renal* or kidney* or nephro* or glomerul* or nephri* or albuminuri* or proteinuria or anuria or ESRD or CKD or ESRF or uremia or uremic or prerenal* or pre-renal* or predialy* or pre-dialy* or pre-esrf or pre-esrd or hyperuremia or uraemia or dialy* or microdialy* or hemodial* or haemodial* or hemodiafiltrat* or hemofiltrat* or haemodiafiltrat* or

haemofiltrat*) 8,310

S1 DE "HEMODIALYSIS" OR DE "KIDNEY diseases" OR DE "KIDNEY failure" 945

Figure S1: Risk of Bias for RCTs

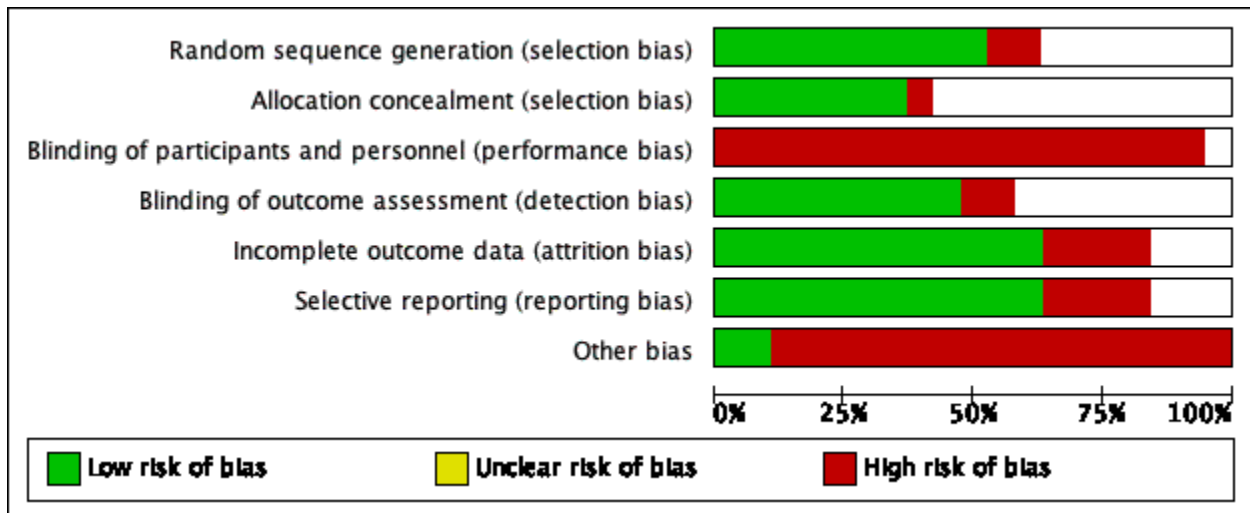


Figure S2a: Meta-analysis of studies examining the effect of intradialytic exercise on cardiac autonomic dysfunction using Heart Rate Variability SDNN

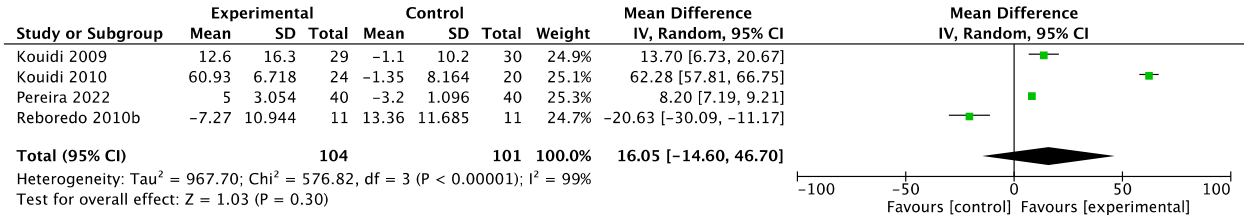


Figure S2b: Meta-analysis of studies examining the effect of intradialytic exercise on cardiac autonomic dysfunction using HRV LF/HF

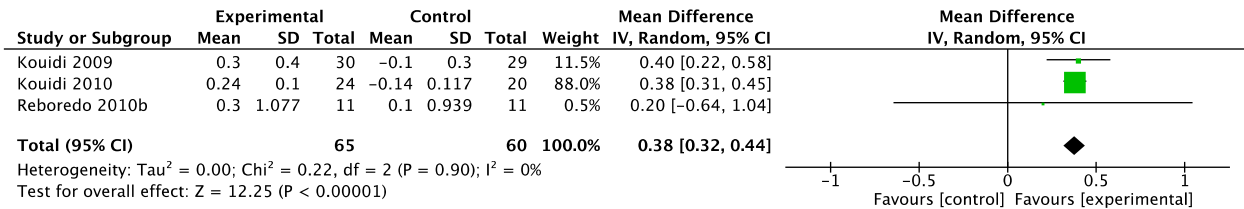


Table S2: Risk of Bias for Non-RCT Studies

Study	Selection				Comparability		Outcome	
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis (there was one study group)	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Anderson et al. 2004	*	*	*	*	-	*	*	*
Chan et al. 2017	*	*	*	*	-	*	-	*
Guio et al. 2017	*	-	*	*	-	*	*	*
Isnard-Rouchon et al. 2017	-	*	*	*	**	*	*	*
Kim et al. 2019	*	*	*	*	-	*	-	*
Mihaescu et al. 2013	*	*	*	*	-	*	*	*
Miller et al. 2002	*	*	*	*	**	*	-	*
Painter et al. 1986	*	*	*	*	-	*	*	*
Thenmozhi et al. 2018	*	*	*	*	**	*	*	*
Moore et al. 1993	*	*	*	*	-	*	-	*

Musavian et al. 2015	*	*	*	*	-	*	-	*
Reboredo et al. 2010	*	*	*	*	-	*	*	*

References

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