Physical Activity in Patients Treated With Peritoneal Dialysis: A Protocol for a Systematic Review

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Abstract

Background: Patients with chronic diseases are known to benefit from exercise. Despite a lack of compelling evidence, patients with end-stage kidney disease treated with peritoneal dialysis are often discouraged from participating in exercise programs that include resistance training due to concerns about the development of hernias and leaks. The actual effects of physical activity with or without structured exercise programs for these patients remain unclear. The purpose of this study is to more completely define the risks and benefits of physical activity in the end-stage kidney disease population treated with peritoneal dialysis.

Methods/design: We will conduct a systematic review examining the effects of physical activity on end-stage kidney disease patients treated with peritoneal dialysis. For the purposes of this review, exercise will be considered a purposive subcategory of physical activity. The primary objective is to determine if physical activity in this patient population is associated with improvements in mental health, physical functioning, fatigue and quality of life and if there is an increase in adverse outcomes. With the help of a skilled librarian, we will search MEDLINE, EMBASE, CINAHL, and Cochrane Central Register of Controlled Trials for randomized trials and observational studies. We will include adult end-stage kidney disease patients treated with peritoneal dialysis that have participated in an exercise training program or had their level of physical activity assessed directly or by self-report. The study must include an assessment of the association between physical activity and one of our primary or secondary outcomes measures. We will report study quality using the Cochrane Risk of Bias Assessment Tool for randomized controlled trials and the Newcastle–Ottawa Scale for observational studies. Quality across studies will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. The results of this review may help to inform guideline development for exercise recommendations specific to this patient population.

Systematic review registration: PROSPERO:CRD42016041695.

Study Protocol
activité physique et l’un de nos critères principal ou secondaire. La qualité des études retenues sera évaluée: les essais cliniques contrôlés randomisés seront évalués à l’aide de l’outil Cochrane qui mesure les risques de biais, et les études observationnelles le seront avec l’échelle de Newcastle — Ottawa. De même, la qualité des données recueillies au cours de l’étude sera évaluée au moyen de la méthodologie GRADE. Les résultats de cet examen pourront guider l’élaboration de lignes directrices et des recommandations pour la pratique d’une activité physique chez cette population de patients spécifique.

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Keywords
peritoneal dialysis, exercise, physical activity, systematic review, protocol

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What was known before

Patients with end stage kidney disease have a greater risk of dying from cardiovascular disease compared to age and sex matched controls from the general population. They are also at increased risk to develop functional impairment associated with falls and fractures that impacts their quality of life and ability to maintain independence. Patients with other chronic diseases and the frail elderly benefit from aerobic and resistance exercise programs. Despite a lack of compelling evidence, patients with end-stage kidney disease treated with peritoneal dialysis are often discouraged from participating in resistance training due to concerns about developing hernias and leaks. The actual effects of physical activity with or without structured exercise programs for these patients remain unclear.

What this adds

This systematic review will highlight our current understanding of the benefits and risks of physical activity including structured exercise programs in patients with end stage kidney disease treated with peritoneal dialysis. Future directions for research will be suggested.

Background

The incidence of end-stage kidney disease (ESKD) has steadily increased in Canada over the previous decade. There were 5333 newly treated patients with ESKD in Canada in 2013—a figure that increased from just over 3000 in 1994. Of these patients, 96% were initially started on dialysis, with about a 4:1 hemodialysis (HD) to peritoneal dialysis (PD) ratio. Although HD has consistently been the primary treatment modality for patients presenting with ESKD, PD has remained the treatment of choice for about 30% of patients since 2004. The 2 treatment modalities are very different. Hemodialysis is typically completed 3 times per week for about 4 hours each session by trained personnel in a hospital or clinic environment; PD is usually done independently every day at home. The differences in treatment schedule result in altered risks of extracellular fluid volume expansion that may contribute to shortness of breath and postdialysis fatigue that is more likely to be experienced by HD patients. The time that must be dedicated to treatment for both dialysis modalities is significant and requires that patients prioritize activities that need to be completed in their remaining daytime hours.

Despite all of the advances in the treatment, the prognosis for patients diagnosed with ESKD remains poor. These patients have an 18- to 20-fold increased risk of cardiovascular disease compared with age- and sex-matched controls from the general population. Much of this enhanced cardiovascular risk is related to traditional risk factors such as diabetes mellitus, hypertension, and dyslipidemia. Furthermore, initiation of dialysis has been associated with a significant decline in functional status. A study of nursing home residents demonstrated an increase in the Minimum Data Set-Activities of Daily Living scale from 12 in the 3 months prior to dialysis to 16 at 3 months following initiation with higher numbers indicating greater functional impairment. One year after beginning dialysis, 58% of patients had died, and only 13% had managed to maintain their baseline functional capacity. The increased cardiovascular morbidity, mortality, and loss of function may be amenable to interventions that are focused on active living.

For the purposes of this systematic review, physical activity will be defined as any bodily movement produced by skeletal muscles that result in energy expenditure.
is a subset of physical activity that is planned, structured, and repetitive and is undertaken with the goal of improving or maintaining one or more components of physical fitness. Exercise can be further subdivided into resistance exercise (weights, bands) and aerobic exercise (running, cycling, swimming, dancing). Increases in activity levels, self-reported or measured with an accelerometer, have been associated with a reduced risk of death in ESKD patients treated with HD. Patients with other chronic diseases have been shown to benefit from participation in resistance exercise programs with increases in strength, muscle mass, and cardiovascular fitness. These outcomes may be particularly important in delaying the progression of musculoskeletal disorders and preserving functionality. Aerobic exercise has been associated with improvements in self-esteem, quality of life, aerobic fitness, and percent body fat. Exercise has also been shown to decrease the risk of depression, a problem that exists for ~25% of patients with ESKD. Exercise may improve glycemic control, blood pressure, and serum triglyceride levels, which could cumulatively lower cardiovascular disease (CVD) risk.

Despite guidelines recommending nephrologists encourage patients with ESKD treated with dialysis to increase their activity levels, this is rarely done. This may be due to a number of real or perceived barriers and also uncertainty about the best exercise regimen for patients treated with PD. Although a recent Cochrane review suggested that there were benefits to exercise in patients with chronic kidney disease including patients with ESKD treated with HD and PD, the majority of evidence was from patients treated with HD. In a few studies, PD and HD patients were discussed together, or, in most cases, PD patients were not included. Extrapolation of results from patients treated with HD to patients treated with PD is not justified given the fundamental differences that exist between these groups. Hemodialysis patients are a captive population as they spend several hours each week receiving treatment during which time exercise programs can be tested potentially enhancing participation rates that may not be the same for PD patients who are at home. Peritoneal dialysis patients have undergone abdominal surgery and usually have dialysate in their peritoneal cavity. This last tenant underlies the rationale behind discouraging PD patients from participating in physical activity that involves lifting weight. In 1986, Twardowski et al demonstrated that PD patients have increased intra-abdominal pressures during various activities, including coughing, straining, and weight lifting. According to Laplace’s law, increasing pressure within the peritoneal cavity would create higher tension on the abdominal wall. This, in combination with the surgery for PD catheter placement, has been thought to increase PD patient risk for the development of hernias and leaks.

Given the potential equipoise about physical activity including aerobic and resistance exercise programs in the PD patient population, we will undertake this systematic review of the literature to more completely define the risks and benefits of physical activity in this patient population.

Methods/Design

Research Objectives

We will conduct a systematic review of observational and interventional trials of physical activity in adult patients with ESKD treated with PD. The primary outcomes of interest will focus on patient-centered outcomes of mental health (diagnosis via clinician structured interview or scales such as the Beck Depression Inventory, Hospital Anxiety and Depression Scale, Hamilton Depression Scale), physical functioning (6-minute walk test, stair-climbing capacity, activities of daily living, sit-stand test), fatigue, quality of life (using validated questionnaires such as Short Form [36] Health Survey [SF-36], EuroQuol, Kidney Disease Quality of Life Instrument [KDQOL, and their subscales) and adverse effects (musculoskeletal [MSK] injury, cardiovascular adverse events, hernias, leaks, mortality). Secondary outcomes will include nutritional measures (albumin, prealbumin, Subjective Global Assessment, energy intake, protein intake, body mass index), lipid profile, blood pressure changes, maximum heart rate, resting heart rate, maximal oxygen consumption (peak VO₂), muscle development (morphometrics), cognitive function, and markers of inflammation (serum interleukin 6, lymphocytes, protein catabolic rate).

Types of Studies

This systematic review will include 2 types of studies: (1) intervention trials that examine the effects of different exercise regimens on our stated primary and secondary outcome measures and (2) observational studies that investigate the association between measures of physical activity and our stated outcome measures. Although this approach maximizes the inclusivity of our search, we anticipate several challenges. First, there will likely be substantial heterogeneity with respect to the exercise interventions tested and the measures of physical activity used. For the purposes of our study, we will classify the training programs used in the intervention trials as aerobic, resistance, or combined aerobic/resistance exercise. Second, with such a diverse array of outcomes and likely a limited number of studies, pooling of results is unlikely and will not be attempted.

Search Strategy

A comprehensive electronic search will be conducted using MEDLINE, EMBASE, CINAHL, and Cochrane Central Register of Controlled Trials with the assistance of a librarian experienced in systematic reviews. A structured search strategy will be based on controlled vocabulary and relevant key terms and will be broad to prioritize sensitivity (see Appendix). The references of included articles and existing reviews will be scanned for additional resources.

Study Screening and Inclusion

All titles and abstracts compiled from the search strategy will be screened by 2 independent reviewers. Each study will be
examined for appropriate inclusion and exclusion criteria. If an abstract is absent, the full text will be examined, unless the title alone can confidently exclude the study. Any disagreement between the reviewers at this stage will result in the study proceeding to a full-text review.

**Inclusion Criteria**

The focus of this systematic review will be adult (≥18 years) patients who (1) are diagnosed with ESKD, (2) are treated with PD (continuous cyclic PD, nocturnal intermittent PD, and chronic ambulatory PD), and (3) have some measure of physical activity (aerobic or resistive exercise regimen, pedometer, accelerometer, self-report). We will include all observational prospective and retrospective studies (cross-sectional, case-control, case-report, and cohort) as well as interventional (randomized or nonrandomized) controlled trials. The absolute minimum requirements for interventional exercise regimens will be 30 minutes (aerobic or resistance training), 3 times per week by the end of the study for at least 2 months. Although this amount of exercise is substantially less than that is currently recommended on the Canadian Hypertension and Canadian Diabetes Association Web sites, mortality risk in HD patients was 27% lower in patients who exercised more than 1 time per week.6 Non-English articles will be included.

**Exclusion Criteria**

Studies that include both pediatric and adult patients but fail to separate the 2 will also be excluded unless authors are able to provide more information. We will also exclude studies that report the results of PD and HD patients collectively without separating the results by dialysis modality if we are unable to obtain patient-level data from the authors.

**Data Extraction**

Each study included in the review will undergo standardized data extraction and summarization by 2 independent reviewers to minimize errors and bias.

Eligibility information will be extracted pertaining to study identification (first author, year of publication), study design (type of study, sample size, inclusion and exclusion criteria, nature of physical activity/exercise regimen), and patient population (age, gender, duration of PD). The primary and secondary outcomes of interest will be extracted from the studies as described in the Research Objectives section. We will contact the original authors for missing data, if deemed necessary. Any difference of opinion will be resolved by consensus and discussion with a third investigator.

**Quality Assessment**

Two review authors will independently assess the risk of bias in the included studies. All randomized controlled trials (RCTs) will be evaluated using the Cochrane Risk of Bias Assessment Tool.24 However, it should be noted that due to the nature of the intervention being studied, we do not anticipate participant blinding. Observational studies will be evaluated with the Newcastle-Ottawa Scale.25 The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be used to assess the quality of the evidence presented across the studies for each outcome as recently adopted by the Canadian Society of Nephrology. The GRADE approach considers many factors including the risk of bias in addition to consistency of results across studies, precision of estimates across studies, the magnitude of the effect, and the importance of the outcome.26 The quality of the evidence will be rated as high, moderate, low, or very low for each outcome.

**Analysis Plan**

The extracted data will be presented through a series of tables and text. We will include study identifiers, study design, patient population characteristics, and relevant outcomes as stated earlier. We do not anticipate being able to pool treatment effects in a quantitative analysis based on an anticipated lack of high-quality studies, variable definitions, and measures of activity/exercise and outcomes. For this reason, descriptive methods will be used to present data by outcome.

**Discussion**

In this systematic review, we will assess the benefits and risks of physical activity on adult patients with ESKD treated with PD. Although our methodology has been designed to be inclusive and to minimize selection bias, we do anticipate several limitations: a lack of randomized control trials, methodological heterogeneity, and potentially poor quality of existing studies. As a consequence of these limitations, we anticipate that we will not be able to combine studies for a meta-analysis but rather present our findings using descriptive methods.

As described in the Background section, fewer patients with ESKD are treated with PD than HD. Also PD and HD patients may be grouped together in the results of prior studies, despite being fundamentally different treatment modalities. Therefore, we are concerned about the possibility of finding very few PD-specific studies. We will contact authors in an attempt to get patient-level data to address the second issue.

We also anticipate heterogeneity between studies as there is no standardized exercise regimen for patients with ESKD as exists for patients with postmyocardial infarction.27-29 As such, the type of exercise, intensity, and duration are expected to result in different outcome measures. Particularly, aerobic exercises (light-to-moderate intensity sustained activities) compared with resistive training (short-term high-intensity muscle contractions) could present with highly variable favorable and adverse event profiles. It will be imperative for us to account accordingly for these factors when collecting and analyzing our results. Similarly, we anticipate that physical activity will be assessed in a multitude of different ways with a variety of outcome measures.
Another notable source of heterogeneity will be from the broad nature of our stated outcomes. Our primary outcomes of interest include mental health, functional status, and quality of life in addition to adverse events. Mental health may be assessed by clinical interview or with a number of different scales such as the Beck Depression Inventory or the Hamilton Rating Scale for Depression making pooling of data impossible. The same challenges exist for assessing functional status and quality of life.

Finally, we anticipate that there may be inherent variability in the characteristics of patients who participate in studies focused on exercise interventions. These patients may be more likely than the average ESKD patient to already be engaged in active living practices and hence more comfortable with participating in such studies, potentially confounding the results. It also remains to be seen what the feasibility of exercise interventions will be in an ESKD population with multiple comorbid illnesses and time constraints created by their treatment. Prior studies have consistently demonstrated low rates of exercise in ESKD patients, and as such, any recommendations based on this systematic review will need to address patient barriers to active living.

In summary, our systematic review and meta-analysis will provide insight into the benefits and risks of exercise interventions on patients with ESKD treated with PD. The results could be used to establish concrete, evidence-based guidelines for exercise in this patient population. They will also help identify gaps in knowledge that can be addressed in future studies.

Appendix

Search Strategy

Database: Embase Classic+Embase <1947 to 2016 November 23>, EBM Reviews—Cochrane Central Register of Controlled Trials <October 2016>, Epub Ahead of Print, In-Process, & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

1 exp Peritoneal Dialysis/ (55 794)
2 (peritoneal adj2 dialysis).tw, (53 061)
3 CAPD.tw, (14 990)
4 *Kidney Failure, Chronic/ (80 042)
5. (end stage renal disease* or esrd).tw, (72 283)
6. or/1-5 (191 425)
7 exp Exercise/ (497 969)
8 (running or swimming or jogging or skiing or bicycling or biking or walking or exercis*).tw, (872 482)
9 exp exercise movement techniques/ or exp exercise therapy/ (124 612)
10 yoga.tw, (8612)
11 exp physical endurance/ (59 838)
12 (resistance train* or combination train*).tw, (15 337)
13 exp sports/ (324 127)
14 Motor Activity/ (150 661)
15 physical activit*.tw, (204 217)
16 or/7-15 (1 433 877)
17 6 and 16 (2592)
18 hemodialysis/ not (exp peritoneal dialysis/ or Kidney Failure, Chronic/) (129 751)
19 17 not 18 (2317)
20 19 use ppez (1291) Medline
21 exp Peritoneal Dialysis/ (55 794)
22 (peritoneal adj2 dialysis).tw,kw, (53 734)
23 CAPD.tw,kw, (15 197)
24 *Kidney Failure, Chronic/ (80 042)
25 (end stage renal disease* or esrd).tw,kw, (75 097)
26 or/21-25 (193 800)
27 exp Exercise/ (497 969)
28 (running or swimming or jogging or skiing or bicycling or biking or walking or exercis*)tw,kw, (886 804)
29 exp exercise movement techniques/ or exp exercise therapy/ (124 612)
30 yoga.tw,kw, (8803)
31 exp physical endurance/ (59 838)
32 (resistance train* or combination train*).tw,kw, (16 520)
33 motor activity/ or physical activit*.tw,kw, (330 806)
34 exp sports/ (324 127)
35 or/27-34 (1 439 835)
36 26 and 35 (2686)
37 hemodialysis/ not (exp peritoneal dialysis/ or Kidney Failure, Chronic/) (129 751)
38 36 not 37 (2367)
39 38 use cctr (80) Cochrane
40 peritoneal dialysis/ (47 162)
41 continuous ambulatory peritoneal dialysis/ (22 704)
42 (peritoneal adj2 dialysis).tw, (53 061)
43 CAPD.tw, (14 990)
44 *end stage renal disease/ (66 144)
45 (end stage renal disease* or esrd).tw, (72 283)
46 or/40-45 (178 921)
47 exp *exercise/ (258 213)
48 (running or swimming or jogging or skiing or bicycling or biking or walking or exercis*).tw, (872 482)
49 exp *kinesiotherapy/ (29 126)
50 exp *sport/ (185 076)
51 yoga.tw, (8612)
52 (resistance train* or combination train*).tw, (15 337)
53 exp physical activity/ or physical activit*.tw, (724 206)
54 or/47-53 (1 440 963)
55 54 and 54 (2519)
56 56 hemodialysis/ not (continuous ambulatory peritoneal dialysis/ or peritoneal dialysis/ or end stage renal disease*) (128 113)
Cinahl Complete—November 28, 2016.

| #   | Query                                          | Results |
|-----|------------------------------------------------|---------|
| S1  | Peritoneal N2 dialysis                         | 3 403   |
| S2  | CAPD                                           | 400     |
| S3  | (MM “Kidney Failure, Chronic”)                 | 11 948  |
| S4  | end stage renal disease* OR esrd                | 5683    |
| S5  | S1 OR S2 OR S3 OR S4                          | 17 060  |
| S6  | (MH “Exercise”)                               | 76 389  |
| S7  | TI (running or swimming or jogging or skiing   | 95 106  |
|     | or bicycling or biking or walking or exercis*  |         |
| S8  | (MH “Therapeutic Exercise*”)                   | 37 469  |
| S9  | (MH “Yoga”)                                   | 4967    |
| S10 | TI yoga OR AB yoga                            | 2955    |
| S11 | (MH “Physical Endurance*”)                    | 9280    |
| S12 | (MH “Sports*”)                                | 55 150  |
| S13 | (resistance train* or combination train*)      | 4010    |
| S14 | (MH “Physical Activity”)                      | 25 514  |
| S15 | TI physical activit* OR AB physical activit*    | 33 126  |
| S16 | S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR  | 214 503 |
|     | S13 OR S14 OR S15                             |         |
| S17 | S5 AND S16                                     | 416     |

References

1. Canadian Institute for Health Information. CIHI: annual report 2014-15. http://www.cihiconferences.ca/annualreport2015/index_en. Accessed July 19, 2016.
2. Ramapiya S, Jean LH. Peritoneal dialysis versus hemodialysis: risks, benefits, and access issues. *Adv Chronic Kidney Dis*. 2011;18:428-432.
3. US Renal Data System. 2015 annual data report: end stage renal disease (ESRD) in the United States. https://www.usrds.org/2015/view/Default.aspx. Published 2015. Accessed July 19, 2016.
4. Manjula T, Kenneth EC, Glenn MC, Kristine Y, Seth L, Charles EM. Functional status of elderly adults before and after initiation of dialysis. *N Engl J Med*. 2009;361:1539-1547.
5. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep*. 1985;110(2):126-131.
6. Tentori F, Elder SJ, Thumma J, et al. Physical exercise among participants in the Dialysis Outcomes and Practice Patterns Study (DOPPS); correlates and associated outcomes. *Nephrol Dial Transplant*. 2010;25:3050-3062.
7. Matsuzawa R, Matsunaga A, Wang G, et al. Habitual physical activity measured by accelerometer and survival in maintenance hemodialysis patients. *Clin J Am Soc Nephrol*. 2012;7:2010-2016.
8. Hurley BF, Hanson ED, Sheaff AK. Strength training as a countermeasure to aging muscle and chronic disease. *Sports Med*. 2011;41(4):289-306.
9. Strasser B, Steindorf K, Wiskemann J, Ulrich CM. Impact of resistance training in cancer survivors: a meta-analysis. *Med Sci Sports Exerc*. 2013;45:2080-2090.
10. Johansen KL, Painter PL, Sakkas GK, Gordon P, Doyle J, Shubert T. Effects of resistance exercise training and nandrolone decanoate on body composition and muscle function among patients who receive hemodialysis: a randomized, controlled trial. *J Am Soc Nephrol*. 2006;17:2307-2314.
11. Murtezani A, Ibraimi Z, Bakalli A, Krasniqi S, Disha ED, Kurtishi I. The effect of aerobic exercise on quality of life among breast cancer survivors: a randomized controlled trial. *Am J Cancer Res Ther*. 2014;10:658-664.
12. Courneya KS, Segal RJ, Mackey JR, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *J Clin Oncol*. 2007;25:4396-4404.
13. Palmer S, Vecchio M, Craig JC, et al. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int*. 2013;84:179-191.
14. Johansen KL, Sakkas GK, Doyle J, Shubert T, Dudley RA. Exercise counseling practices among nephrologists caring for patients on dialysis. *Am J Kidney Dis*. 2003;41:171-178.
15. Cynthia D, Kirsten LJ. Barriers to exercise participation among dialysis patients. *Nephrol Dial Transplant*. 2012;27:1152-1157.
16. Johansen KL. Exercise in the end-stage renal disease population. *J Am Soc Nephrol*. 2007;18:1845-1854.
17. Heiwe S, Jacobson SH. Exercise training for adults with chronic kidney disease. *Cochrane Database Syst Rev*. 2011;11:CD003236.

Ethics Approval and Consent to Participate

As this is a systematic review, ethics approval and consent to participate are not required.

Consent for Publication

Consent to Publish was obtained from all authors.

Availability of Data and Materials

Upon completion of the study, data and materials will be available through PROSPERO.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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18. Ellam T, Wilkie M. Peritoneal dialysis. *Medicine*. 2007;35:466-469.
19. Mehrotra R, Boeschoten EW. Current status of peritoneal dialysis. In: Khanna R, Kredit RT, eds. *Nolph and Gokal’s Textbook of Peritoneal Dialysis*. New York, NY: Springer; 2009:19-38.
20. Bargman JM. Hernias in peritoneal dialysis patients: limiting occurrence and recurrence. *Perit Dial Int*. 2008;28:349-351.
21. Albee BJ. Precautions for sports-minded patients on peritoneal dialysis. *ANNA J*. 1995;22:332-333.
22. Twardowski ZJ, Khanna R, Nolph KD, et al. Intraabdominal pressures during natural activities in patients treated with continuous ambulatory peritoneal dialysis. *Nephron*. 1986;44:129-135.
23. Bargman JM. Noninfectious complications of peritoneal dialysis. In: Khanna R, Kredit RT, eds. *Nolph and Gokal’s Textbook of Peritoneal Dialysis*. New York, NY: Springer; 2009:571-610.
24. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration’s tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
25. Wells GA, Shea B, O’Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. The Ottawa Hospital. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Published 2016. Accessed July 19, 2016.
26. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64(4):401-406.
27. Anderson L, Thompson DR, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev*. 2016;1:CD001800.
28. Thompson PD. Exercise prescription and proscription for patients with coronary artery disease. *Circulation*. 2005;112(15):2354-2363.
29. Piotrowicz R, Wolszakiewicz J. Cardiac rehabilitation following myocardial infarction. *Cardiol J*. 2008;15(5):481-487.
30. Johansen KL, Chertow GM, Ng AV, et al. Physical activity levels in patients on hemodialysis and healthy sedentary controls. *Kidney Int*. 2000;57:2564-2570.
31. Painter P, Carlson L, Carey S, Paul SM, Myll J. Physical functioning and health-related quality-of-life changes with exercise training in hemodialysis patients. *Am J Kidney Dis*. 2000;35:482-492.
32. Tawney KW, Tawney PJ, Hladik G, et al. The life readiness program: a physical rehabilitation program for patients on hemodialysis. *Am J Kidney Dis*. 2000;36:581-591.