



# Timed Stair-Climbing as a Surrogate Marker for Sarcopenia Measurements in Predicting Surgical Outcomes

Samantha Baker<sup>1</sup> · Mary Glen Waldrop<sup>1</sup> · Joshua Swords<sup>1</sup> · Thomas Wang<sup>1</sup> · Martin Heslin<sup>1</sup> · Carlo Contreras<sup>1</sup> · Sushanth Reddy<sup>1</sup> 

Received: 22 August 2018 / Accepted: 29 October 2018 / Published online: 3 December 2018  
© 2018 The Society for Surgery of the Alimentary Tract

## Abstract

**Background** Estimating sarcopenia by measuring psoas muscle density (PMD) has been advocated as a method to accurately predict post-operative morbidity. The aim of the present study was to determine whether the Timed Stair Climb (TSC) could be used to replace PMD measurements in predicting morbidity.

**Methods** Patients were prospectively enrolled from March 2014–2015 and were eligible if they were undergoing an abdominal operation. PMD was measured using pre-operative CT scans obtained within 90 days of surgery. Ninety-day complications were assessed using the Accordion Severity Grading System. Multivariable analysis was performed to identify risk factors associated with operative morbidity.

**Results** Of the patients, 298 were enrolled and completed TSC prior to undergoing an operation. Using the According Grading System, a grade 2 or higher complication occurred in 72 (24.2%) patients with 8 (2.7%) deaths. There was an indirect relationship between PMD and TSC ( $P < 0.0001$ ) and a direct relationship between TSC and complications ( $P = 0.04$ ). On multivariable analysis decreasing PMD ( $P = 0.018$ ) and increasing TSC ( $P = 0.026$ ) were predictive of post-operative morbidity. Receiver operating characteristic curves demonstrated that the TSC was superior to both the ACS NSQIP Risk Calculator and PMD in predicting outcomes (TSC vs. PMD,  $P = 0.012$ ; PMD vs. ACS NSQIP,  $P = 0.013$ ; TSC vs. ACS NSQIP,  $P < 0.0001$ ).

**Conclusion** TSC, PMD, and the ACS NSQIP calculator are all useful tools; however, the TSC is superior in predicting post-operative morbidity.

**Keywords** Sarcopenia · Functional outcome · Abdominal surgery · Surgical risk

## Introduction

Surgeons must be able to weigh the risk-to-benefit ratio for each patient undergoing an operation. Historically, this was accomplished without clear-cut definitions, and patients would have to pass the “eyeball test” before being taken to the operating room. With increasing research, technology, and

diagnostic capabilities, several studies have demonstrated that there is a relative increase in post-operative complications associated with individual medical conditions such as congestive heart failure,<sup>1</sup> tobacco use,<sup>2</sup> and chronic kidney disease<sup>3</sup> among others.

In order to better quantify the relative risk of each individual patient for each operation, the American College of Surgeons developed the National Surgical Quality Improvement Project (ACS NSQIP) Surgical Risk Calculator.<sup>4</sup> This calculator estimates surgical risk by combining pre-existing medical conditions in a single model with different procedure types. The ACS NSQIP Surgical Risk Calculator has been criticized due to its reliance on categorical variables in risk stratification creating discussion about its ability to overestimate or underestimate risk.<sup>5</sup>

Some investigators have turned to a more patient specific measure in attempts to create a better predictor of post-

---

This manuscript was presented at the 2017 Academic Surgical Congress in Las Vegas, NV.

---

✉ Sushanth Reddy  
sreddy@uabmc.edu

<sup>1</sup> Division of Surgical Oncology, University of Alabama at Birmingham, BDB 607 1808 7th Avenue South, Birmingham, AL 352433-3411, USA

operative complication by measuring an individual's physical performance or muscle measurements.<sup>6</sup> These included the timed up and go (TUG) where patients had to walk a short distance while being timed. TUG was found to be most predictive when combined with other calculators.<sup>7</sup> Other investigators have turned to imaging to assess overall physical status and lean muscle mass by measuring psoas muscle density (PMD) on cross-sectional imaging.<sup>6, 8–10</sup> It has been previously demonstrated that PMD measurements on imaging have outperformed the ACS NSQIP Surgical Risk Calculator in predicting outcomes.<sup>11</sup>

Combinations of several of these indices appear to be quite effective in predicting outcomes;<sup>10</sup> however, this method of risk stratification may be too cumbersome for a busy general surgeon to use in clinical practice. We had previously demonstrated that a timed stair climb (TSC) provides measurable stress and is superior to the ACS NSQIP Surgical Risk Calculator in predicting morbidity and length of stay.<sup>5</sup> We hypothesized that TSC was a surrogate for axial muscle strength and may be used in lieu of PMD when estimating surgical risk. The aim of the present study was to determine whether TSC is a marker of axial muscle strength and if it can be used to replace PMD measurements in predicting morbidity.

## Materials and Methods

Appropriate IRB approval was obtained, and patients were recruited prospectively for our study from March 2014 to May 2015. Patients were eligible for the study if they were over 18 years of age, their Surgical Oncologist deemed them an appropriate surgical candidate, and the operation was planned under general anesthesia with planned entry into the peritoneum. Patients were excluded if they underwent an emergent operation. After enrollment patients underwent a timed stair climb test within the 30 days prior to their operation. The stair climb test consisted of the patients walking down and then up a single flight of 12 stairs while being timed. The flight of stairs used met the criteria for a standard set of stairs and those who could not complete the test were assigned a time of 100 s. Psoas muscle measurements were obtained by a single-blinded physician using the venous phase of an enhanced CT scan. All CT scans used were within 90 days prior to the index operation date and had varying slices between 0.1 and 1-mm thickness. The psoas muscle measurements were taken at the level of L3 when both the right and left transverse processes were visible. Both the total psoas muscle area (TPA) and Hounsfield unit average calculation (HUAC) were used to assess muscle amount and density, respectively. HUAC was calculated by the formula seen in Fig. 1. We then used the cross-sectional area and divided it by the height in meters squared of the individual. For the

$$HUAC = \left( \frac{RHU \times RPA}{TPA} + \frac{LHU \times LPA}{TPA} \right) / 2$$

Fig. 1 HUAC formula

complication analysis, the Accordion Severity Grading System was used and complications grade 2 or higher were recorded retrospectively.<sup>12</sup> Briefly, grade 1 complications are considered minor complications that involve bedside procedures such as an nasogastric tube (NGT) insertion, grade 2 complications are considered moderate complications and involve blood transfusions or need for total parenteral nutrition (TPN), grade 3 complications are severe and require intervention without general anesthesia, grade 4 complications are also severe but require intervention with general anesthesia, grade 5 complications are severe and involve organ system failure, and a post-operative death would be a grade 6 complication.

Timed stair climb was then correlated to complication rate and compared to psoas muscle density. Univariable differences in patient population characteristics by post-operative complication status were assessed using *t* test and two-sided Fisher's exact test statistics. Univariable and multivariable analyses were performed to identify pre-operative risk factors associated with operative morbidity using logistic regression models. Receiver operator curves were constructed to compare the ACS-NSQIP Surgical Risk Calculator tool, the timed stair climb test, and psoas muscle measurements. All statistical analyses were performed with STATA SE 13.0 (StataCorp) and GraphPad Prism 5 (GraphPad Software Inc.) software. Statistical threshold for significance was set at  $\alpha = 0.05$  for all tests.

## Results

We prospectively enrolled 298 patients in our study. All 298 patients attempted TSC prior to undergoing elective surgery. Of those patients, 15 were excluded from a complication analysis due to either their surgery being canceled or the peritoneum not being entered in the operation. All patients were included in the comparison of their timed stair climb with psoas muscle measurements. Of the patients, 283 underwent an abdominal surgery for various surgical oncology indications; these included open and laparoscopic operations in the following subcategories: 78 colorectal (27%), 46 pancreatic (16%), 35 gastro-esophageal (12%), 30 liver (11%), 29 small bowel (10%), 29 retroperitoneal (10%), and 36 other (13%). Of the 298 patients included in the study, 46% were male, 75% were Caucasian, and the median age was 60 years.

## Complications

A grade 2 or higher complication occurred in 72 (25.4%) patients with 8 (2.8%) deaths. Table 1 depicts the frequency

**Table 1** Types and frequency of post-operative complication

Complication	N (%)
Need for parenteral nutrition	12 (4.2)
Re-admission to hospital or ICU	10 (3.5)
Post-operative pancreatic fistula	8 (2.8)
Afib/flutter	7 (2.5)
Need for blood transfusion	7 (2.5)
SSI	5 (1.8)
Intraabdominal abscess	5 (1.8)
NSTEMI	3 (1.1)
Delayed gastric emptying	4 (1.4)
GI bleed	4 (1.4)
PNA	2 (0.7)
Flap necrosis	2 (0.7)
Need for re-operation	2 (0.7)
Wound dehiscence	2 (0.7)
SBO	2 (0.7)
AKI	1 (0.4)
EC fistula	1 (0.4)
Chyle leak	1 (0.4)
CVA	1 (0.4)
Perianal abscess	1 (0.4)
Re-intubation	1 (0.4)
MI	1 (0.4)
Death	8 (2.8)
Total	90

Note that some patients had multiple complications

of complications, with need for TPN being the most common complication ( $N = 12$ , 4.2%) and re-admission to the hospital or escalation of care the second most common ( $N = 10$ , 3.5%). TPN use was at the discretion of each individual surgeon. The reasons for TPN were inability to tolerate oral diet for at least 5 days ( $N = 9$ ), high-output pancreatic fistula ( $N = 2$ ), and

chyle leak ( $N = 1$ ). Table 2 illustrates the demographics and clinical characteristics of the group of patients that had a complication compared to the group of patients that did not. Patients who experienced a complication were older and were more likely to have COPD and less likely to be Caucasian.

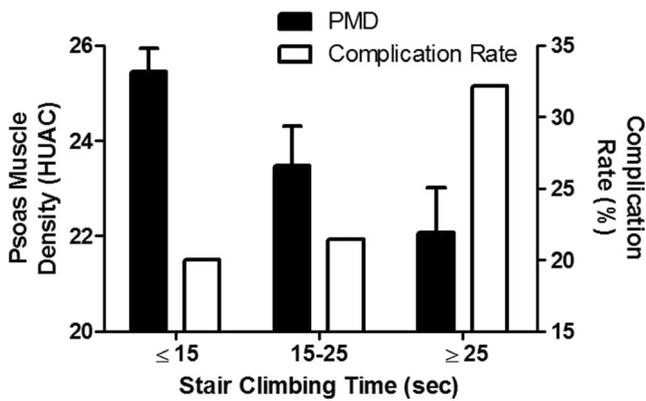
Patients who had a surgical morbidity also had a slower stair climbing time and a smaller psoas muscle as measured by the HUAC. There was no difference of TPA between the two groups. There was a direct relationship between TSC and complication rate (Fig. 2;  $P = 0.04$ ), showing that as TSC time increased so did the rate of complications. Furthermore, there was an indirect relationship between TSC and PMD (Figure 2;  $P < 0.0001$ ), showing that as psoas muscle density decreased the time needed to complete the stair climb increased.

**Complication Predictive Models**

Interestingly, univariable analysis demonstrated increasing age, non-Caucasian race, presence of COPD, increased TSC, decreased HUAC, and the ACS NSQIP pre-operative risk calculation score were all statically significant factors in predicting post-operative outcomes (Table 3). On multivariable analysis the decreasing PMD as measure by HUAC ( $P = 0.036$ ), increasing TSC ( $P < 0.0001$ ), and ACS NSQIP calculator score ( $P < 0.0001$ ) were predictors of post-operative morbidity; the presence of COPD and Caucasian race were no longer statistically significant (Table 4). Receiver operator characteristic curves were constructed for all three models to test the validity of the tool to predict post-operative outcomes. All three tests were useful predictors of post-operative

**Table 2** Comparison between patients who experienced complications and those who did not

Variable	Complication (N = 72)	No complication (N = 211)	P value
Age (median, years)	64.0	57.9	0.0006
Sex (female)	61%	50%	0.13
Race (Caucasian)	69%	80%	0.10
Tobacco use	58%	54%	0.58
Hypertension	63%	55%	0.27
Diabetes mellitus	24%	22%	0.75
Coronary artery disease	11%	11%	1.0
Congestive heart failure	3%	3%	1.0
Chronic obstructive pulmonary disease	11%	4%	0.05
Hypercholesterolemia	40%	30%	0.14
Alcohol abuse	6%	9%	0.46
Body mass index (median)	28.3	28.3	0.54
Stair climbing time (median, s)	26.5	15.0	< 0.0001
Albumin < 3.4 g/dL	19%	11%	0.08
HUAC (median)	22.4	24.2	0.02
TPA (median)	13.7	13.5	0.26



**Fig. 2** Relationship between TSC and complication rate compared with PMD

morbidity (Fig. 3). AUC calculations demonstrated that PMD was superior to the NSQIP calculator in predicting post-operative complication rates ( $P=0.013$ ). TSC was superior to both the PMD ( $P=0.012$ ) and the NSQIP calculator ( $P<0.0001$ ).

## Discussion

This study demonstrated the utility of timed stair climb as a surrogate for psoas muscle measurements in predicting surgical outcomes in pre-operative setting for all patients undergoing elective abdominal surgery. Patients who had a longer stair climbing time had less dense psoas muscles and more complications. Timed stair climb was superior to psoas muscle density measurements and NSQIP surgical risk calculator in predicting surgical outcomes.

Historically, it has been known that surgical outcomes are dependent on many variables including patient factors and the type of surgery. Patient factors until recently had been somewhat vague and difficult to quantify with much of the ability to assess a patient's readiness for surgery relying on a surgeon's gestalt. Recently, there have been several model calculators introduced to help surgeons discuss estimated surgical risk with patients such as the ACS NSQIP Surgical Risk Calculator. These data are collected from 393 NSQIP hospitals across the USA over 3.5-year time period with over 1.4 million patients enrolled. A model was created using the CPT for the procedure and 21 pre-operative categorical risk factors that predicts 8 different postoperative outcomes. This method has inherent limitations being drawn from a large database and the yes/no binary answer to the categorical pre-operative risk factors without considering the degree of disease state.<sup>4</sup>

A trendy and in vogue method currently is to use psoas muscle measurements to predict surgical outcomes. This is a relatively new concept and has become increasing more utilized across all surgical specialties since it is easily defined and reproducible. Psoas muscle measurements are made at the level of the L3 vertebra, and the muscle area is compared to the visceral fat content within the same level. Several studies have demonstrated that sarcopenia leads to worse surgical outcomes in a variety of patients including liver<sup>9</sup> and pancreatic resections.<sup>8</sup> While these data are, in theory, easily reproducible, it requires advanced radiologic software and dedicated time of the surgeon. The overall process of measuring and calculating psoas muscle measurements is time-consuming. Notably, an observation seen by others about psoas muscle measurements is that density seems to be more important than cross-sectional area in predicting outcomes that just muscle

**Table 3** Univariable analysis for predictive factors of surgical outcomes

Variable	Odds ratio	95% confidence interval	<i>P</i> value
Caucasian race	0.582	0.318–1.063	0.078
Age	1.040	1.016–1.064	0.001
TPA	0.971	0.923–1.022	0.262
HUAC	0.937	0.889–0.987	0.014
Stair time	1.044	1.026–1.063	<0.0001
Tobacco use	1.177	0.684–2.024	0.556
Alcohol abuse	0.594	0.195–1.809	0.360
Hypertension	1.400	0.801–2.434	0.238
Hypercholesterolemia	1.534	0.895–2.767	0.115
Diabetes mellitus	1.112	0.588–2.105	0.743
Coronary artery disease	1.062	0.450–2.506	0.892
Congestive heart failure	0.966	0.190–4.99	0.996
Chronic obstructive pulmonary disease	2.751	1.018–7.433	0.046
Body mass index	0.986	0.941–1.032	0.534
Albumin	0.639	0.342–1.195	0.161
ACS NSQIP predicted any complication	1.042	1.030–1.116	<0.0001

**Table 4** Multivariable analysis for predictors of post-operative outcomes

Variable	Odds ratio	95% confidence interval	<i>P</i> value
Age	1.049	0.887–1.060	0.18
Caucasian race	0.336	0.150–0.631	0.018
COPD	0.857	0.188–3.300	0.921
HUAC	0.934	0.875–0.988	0.044
Stair time	1.033	1.019–1.057	< 0.0001
ACS NSQIP predicted any complication	1.042	1.030–1.116	< 0.0001

area.<sup>11</sup> We demonstrated that PMD measured by HUAC is a significant predictor of surgical outcome; however, the total psoas muscle area was not. This may illustrate the point that quality of the muscle or the density is more important than the overall area or quantity of muscle. Furthermore, we divided the cross-sectional area of the muscle by the individual's height in meters squared. Obese people tend to have a larger TPA due to the increased muscle needed for axial strength, but not necessarily better muscle quality.<sup>10</sup> This study demonstrated that there was an inverse relationship between PMD and stair climbing time. Thus, TSC is a surrogate for PMD measurements.

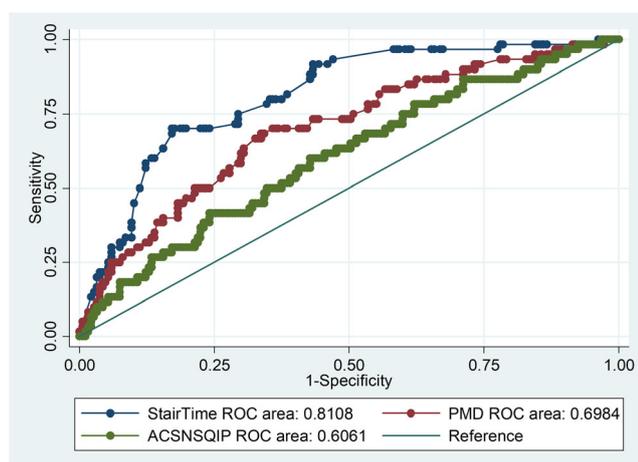
We did not address underlying orthopedic issues in assessing patient fitness for surgery. The effect of arthritis and other chronic muscle/joint issues on functional status have been well extensively studied.<sup>13–15</sup> Current algorithms assessing cardiovascular risk are heavily influenced by patients' subjective symptoms of angina or dyspnea on exertion.<sup>16</sup> Patients with poor ambulation will therefore not report any such symptoms as they do not exert themselves sufficiently to experience them. Subsequently, these patients

will not undergo appropriate testing for cardiovascular disease but remain at higher risk. These conditions lead to more sedentary lifestyles and to increased risk of sarcopenia.<sup>17</sup> We, therefore, believe that psoas muscle and objective functional assessments will prove to be superior to traditional methods for estimating surgical risk.

The complication rate in our study was comparable to the other groups with a rate of 20–25%.<sup>18</sup> Interestingly, Caucasian race was protective and people who were non-Caucasian were more likely to have a post-operative complication in all analyses. The vast majority of the patients in our study were Caucasian. This finding may be due to a selection bias of patients in the study or could be indicative of a racial disparity. The role of race in surgical outcome has been well established.<sup>19</sup>

There are linear relationships between TSC and HUAC with surgical complications. Neither defines a cutoff point for acceptable surgical risk—these tools still require surgeon judgment before an operation. The question arises whether either of these two measures can be modified, thus reducing surgical risk. Most of the patients in our study had cancer indication for surgical intervention, and thus, while an elective planned operation, it was not a surgery that could be postponed for months to attempt to modify certain risk factors. Other investigators have found that cancer itself is a risk for the development of sarcopenia and the degree of psoas muscle loss correlates with cancer stage.<sup>20</sup> Previous attempts at prehabilitation have thus far been unsuccessful in improving post-operative outcomes.<sup>21, 22</sup> PMD and (perhaps) TSC may not be modifiable parameters in cancer patients. These patients may need to assume a greater risk than others or be subjected to other non-operative therapies (e.g., radiation therapy or systemic therapy) if deemed too great of surgical risk. There are several prospective studies looking to assess the role of prehabilitation in the surgical cancer patient.<sup>23, 24</sup>

The elective non-cancer surgical patient may benefit from improving functional status prior to an operation. Others have demonstrated that a course of pre-operative exercise is effective in improving outcomes following anterior cruciate ligament repair<sup>25</sup> and joint replacement surgery.<sup>26</sup> A recent systematic review and meta-analysis did demonstrate the



**Fig. 3** ROC curves for TSC vs. PMD vs. NSQIP calculator. Stair time vs. PMD,  $P = 0.012$ ; PMD vs. ACSNSQIP,  $P = 0.013$ ; PMD vs. ACS NSQIP,  $P < 0.0001$

effectiveness of pre-habilitation on abdominal surgery. The authors did show that pre-habilitation was associated with improved overall morbidity and pulmonary specific morbidity but did not affect hospital length of stay. Only 9 studies and 435 operations were included in this analysis; it appears to also include a mix of cancer and non-cancer patients.<sup>27</sup> TSC and PMD may be effective in identifying high-risk non-cancer surgical patients; further studies will be needed to determine whether pre-habilitation can modify both of these variables and surgical risk.

All three risk assessment tools are effective in predicting surgical outcome; however, the stair climbing time is superior to both psoas muscle measurements and the ACS NSQIP Surgical Risk Assessment Calculator in predicting complications across a wide variety of abdominal surgical procedures.

## Conclusions

Both TSC and PMD are excellent predictors of post-operative morbidity in this population. TSC appears to be a surrogate for axial muscle strength measured by PMD. TSC is an easy tool to administer in lieu of PMD when considering patient outcomes.

## Compliance with Ethical Standards

All authors have contributed substantially to the conception, design, acquisition, analysis, or interpretation of the data. In addition, all authors have participated in the critical revision and approval of the final manuscript.

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## References

- Caulley, L., et al., Risk factors for postoperative complications in total thyroidectomy: A retrospective, risk-adjusted analysis from the National Surgical Quality Improvement Program. *Medicine (Baltimore)*, 2017. 96(5): p. e5752.
- Martin, A.N., et al., Morbidity and Mortality After Gastrectomy: Identification of Modifiable Risk Factors. *J Gastrointest Surg*, 2016. 20(9): p. 1554–64.
- Kuo, F.C., et al., Chronic Kidney Disease Is an Independent Risk Factor for Transfusion, Cardiovascular Complication, and Thirty-Day Readmission in Minimally Invasive Total Knee Arthroplasty. *J Arthroplasty*, 2017. 32(5): p. 1630–1634.
- Bilimoria, K.Y., et al., Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. *J Am Coll Surg*, 2013. 217(5): p. 833–42.e1–3.
- Reddy, S., et al., Timed Stair Climbing Is the Single Strongest Predictor of Perioperative Complications in Patients Undergoing Abdominal Surgery. *J Am Coll Surg*, 2016. 222(4): p. 559–66.
- Makary, M.A., et al., Frailty as a predictor of surgical outcomes in older patients. *J Am Coll Surg*, 2010. 210(6): p. 901–8.
- Robinson, T.N., et al., Slower walking speed forecasts increased postoperative morbidity and 1-year mortality across surgical specialties. *Ann Surg*, 2013. 258(4): p. 582–8; discussion 588–90.
- Peng, P., et al., Impact of sarcopenia on outcomes following resection of pancreatic adenocarcinoma. *J Gastrointest Surg*, 2012. 16(8): p. 1478–86.
- Peng, P.D., et al., Sarcopenia negatively impacts short-term outcomes in patients undergoing hepatic resection for colorectal liver metastasis. *HPB (Oxford)*, 2011. 13(7): p. 439–46.
- Buettner, S., et al., Inclusion of Sarcopenia Outperforms the Modified Frailty Index in Predicting 1-Year Mortality among 1,326 Patients Undergoing Gastrointestinal Surgery for a Malignant Indication. *J Am Coll Surg*, 2016. 222(4): p. 397–407.e2
- Sur, M.D., et al., Radiographic Sarcopenia and Self-reported Exhaustion Independently Predict NSQIP Serious Complications After Pancreaticoduodenectomy in Older Adults. *Ann Surg Oncol*, 2015. 22(12): p. 3897–904.
- Strasberg, S.M., D.C. Linehan, and W.G. Hawkins, The accordion severity grading system of surgical complications. *Ann Surg*, 2009. 250(2): p. 177–86.
- Al-Zahrani, K.S. and A.M. Bakheit, A study of the gait characteristics of patients with chronic osteoarthritis of the knee. *Disabil Rehabil*, 2002. 24(5): p. 275–80.
- Ikutomo, H., et al., Gait Abnormality Predicts Falls in Women After Total Hip Arthroplasty. *J Arthroplasty*, 2018. 33(10): p. 3215–3219.
- Iijima, H., et al., Biomechanical characteristics of stair ambulation in patients with knee OA: A systematic review with meta-analysis toward a better definition of clinical hallmarks. *Gait Posture*, 2018. 62: p. 191–201.
- Multimodality Writing Group for Stable Ischemic Heart, D, et al., ACCF/AHA/ASE/ASNC/HFSA/HRS/SCAI/SCCT/SCMR/STS 2013 multimodality appropriate use criteria for the detection and risk assessment of stable ischemic heart disease: a report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Failure Society of America, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, and Society of Thoracic Surgeons. *J Card Fail*, 2014. 20(2): p. 65–90.
- Gianoudis, J., C.A. Bailey, and R.M. Daly, Associations between sedentary behaviour and body composition, muscle function and sarcopenia in community-dwelling older adults. *Osteoporos Int*, 2015. 26(2): p. 571–9.
- Zhuang, C.L., et al., Sarcopenia is an Independent Predictor of Severe Postoperative Complications and Long-Term Survival After Radical Gastrectomy for Gastric Cancer: Analysis from a Large-Scale Cohort. *Medicine (Baltimore)*, 2016. 95(13): p. e3164.
- Ravi, P., et al., Racial/Ethnic Disparities in Perioperative Outcomes of Major Procedures: Results From the National Surgical Quality Improvement Program. *Ann Surg*, 2015. 262(6): p. 955–64.
- Zhang, G., et al., Incidence and risk factor analysis for sarcopenia in patients with cancer. *Oncol Lett*, 2016. 11(2): p. 1230–1234.
- Gillis, C., et al., Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology*, 2014. 121(5): p. 937–47.

22. Li, C., et al., Impact of a trimodal prehabilitation program on functional recovery after colorectal cancer surgery: a pilot study. *Surg Endosc*, 2013. 27(4): p. 1072–82.
23. Dunne, D.F., et al., Randomized clinical trial of prehabilitation before planned liver resection. *Br J Surg*, 2016. 103(5): p. 504–12.
24. Loughney, L., et al., Physical activity levels in locally advanced rectal cancer patients following neoadjuvant chemoradiotherapy and an exercise training programme before surgery: a pilot study. *Perioper Med (Lond)*, 2017. 6: p. 3.
25. Shaarani, S.R., et al., Effect of prehabilitation on the outcome of anterior cruciate ligament reconstruction. *Am J Sports Med*, 2013. 41(9): p. 2117–27.
26. Wang, L., et al., Does preoperative rehabilitation for patients planning to undergo joint replacement surgery improve outcomes? A systematic review and meta-analysis of randomised controlled trials. *BMJ Open*, 2016. 6(2): p. e009857.
27. Moran, J., et al., The ability of prehabilitation to influence postoperative outcome after intra-abdominal operation: A systematic review and meta-analysis. *Surgery*, 2016. 160(5): p. 1189–1201.