Journal of Frailty, Sarcopenia and Falls

Mini Review

Frailty assessment and postoperative complications in urologic oncology operations

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Abstract

Major urologic oncology procedures such as radical cystectomy (RC), radical prostatectomy (RP), radical nephroureterectomy (RNU) and radical or partial nephrectomy are the gold standard operations for the treatment of urological malignancies not suitable to be dealt with using minimal invasive procedures such as transurethral resection or other conservative approaches. However, these surgical procedures carry significant risk of complications, especially in elderly and frail patients. The purpose of this review is to highlight the use of a wide variety of preoperative frailty and health status indexes and calculators. Recent data from large population based studies confirm that these calculators can assist physicians and urologists to predict the postoperative morbidity of patients undergoing major operations. Moreover, these frailty calculators can help urologists choose the most suitable and safe treatment for every individual patient. However, the absence of widely accepted specific urologic oncology calculators to predict the association between frailty and postoperative complications emphasizes the necessity for the use of a combination of calculators.

Keywords: Frailty, Frailty calculator, Frailty index, Postoperative complications, Urologic oncology operations

Introduction

Worldwide, population aging is a serious and intriguing issue for the medical community. The rise in the aging population is associated with vulnerability[1]. The word frailty refers to a late life phenotype which concerns a group of declines in functioning among multiple systems of the human body. This situation can definitely increase the risk for disability and mortality[1]. Frail people are at higher risk of cardiovascular disease, depression and reduction in their quality of life[2]. This syndrome can also affect endocrine and respiratory systems as well as the skeletal muscle[3]. After all, the determinants of frailty syndrome include reduction in physical activity, malnutrition, sarcopenia, polypharmacy (the use of at least five drugs simultaneously), depression, cognitive disorders and lack of social support[4]. Frailty is associated with increased costs of hospitalization due to postoperative complications and healthcare resource utilization[4].

There is a higher incidence of urological malignancies in the elderly and subsequently they undergo elective urological procedures. Older adults are at the highest risk of poor surgical outcomes, because of comorbidity and frailty. A large retrospective cohort study in 2019 using 92,999 patients who underwent radical cystectomy or minimally invasive or open radical prostatectomy, radical nephrectomy or partial nephrectomy, showed that frailty in major urologic oncology procedures is associated with greater healthcare resource utilization (HRU) and surgical morbidity[5]. An increase in each frailty category was independently

The authors have no conflict of interest.

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Edited by: *Dawn Skelton*

Accepted *21 July 2020*

PREOPERATIVE ASSESSMENT INDEXES	CATEGORY EVALUATED
G8 score	Health status. Evaluates 1. decline of food intake, 2. weight loss, 3. mobility, 4. Neuropsychological problems, 5. BMI, 6. more or less than 3 prescription drugs, 7. Age, 8. comparison with other people of the same age[14-15].
sFI frailty index	Frailty. 1. diabetes mellitus, 2. functional status, 3. history of chronic obstructive pulmonary disease, 4. history of congestive cardiac failure, and 5. hypertension requiring treatment[9].
Johns Hopkins frailty assessment calculator	Frailty. Five phenotypic criteria: unintentional weight loss, exhaustion, low energy expenditure, low grip strength, and/or slowed walking speed[21].
CGA	Frailty functional status, fatigue, comorbidity, cognition, mental health, social support, nutrition and geriatric syndromes (e.g. dementia, delirium, falls, incontinence, osteoporosis or spontaneous fractures, neglect or abuse, failure to thrive, constipation, polypharmacy, pressure ulcers, and sarcopenia)[23].
ASA physical status classification	Health status. Assessing the fitness of patients before surgery five classes (I to V)[11,14].
mini-COG assessment	Cognitive status. Consists of two components, a 3-item recall test for memory and a simply scored clock drawing test[14,18].
Karnofsky score and ECOG performance status	Physical function. Performance status. ECOG 0-5, Karnofsky score 0-100[14,19-20].
CISR-G and CCI	Comorbidities. CISR-G 14 categories. CCI 17 categories, Predicts 10-year survival in patients[14,16-17].

Table 1. Most widely used preoperative frailty assessment indexes for the evaluation of patients before major urologic oncology operations. *BMI: Body Mass Index, G8: Geriatric 8, sFI: simplified five-item, CGA: Comprehensive Geriatric Assessment, ASA: American Society of Anesthesiologists, mini-COG: Mini-Cognitive, ECOG: Eastern Cooperative Oncology Group, CISR-G: Cumulative Illness Score Rating-Geriatrics, CCI: Charlson Comorbidity Index.*

associated with prolonged length of stay, more discharges to continuing care and unplanned readmissions within 30 days[5]. A preoperative assessment of frailty and optimization of its parameters can reduce postoperative morbidity in these patients[6-8], however a wide variety of preoperative frailty and health status indexes and calculators exist and are being used worldwide by physicians. This paper reviews these tools and makes recommendations for future frailty assessment in the context of urological oncology surgery.

Available indexes for prediction of postoperative complications in urologic oncology operations

Radical cystectomy

Many studies have introduced a variety of frailty indexes to predict complications after severe oncology operations. A simplified five-item frailty index (sFI) created by Sathianathen NJ et al. in 2019 showed a strong correlation between frailty and radical cystectomy outcomes, including in the elderly (>65 years)[9]. The components of sFI include history of diabetes mellitus, functional status, history of chronic obstructive pulmonary disease, history of congestive cardiac failure, and hypertension requiring treatment. To calculate the sFI, the presence of each variable was attributed 1 point, with a maximum score of 5 possible[9].

This index was compared to the extended 11-item frailty index, NSQIP risk calculator (National Surgical Quality Improvement Program)[10] and the ASA score (American Society of Anesthesiologists)[11]. Individuals with sFI score 3+ had a greater likelihood of experiencing a major complication and the tool had equal predictive ability to the more complex calculators[9].

A study by Froehner M et al. in March 2020, aimed to find the best tool to identify patients at risk for 90-day or premature long-term non-bladder cancer mortality after radical cystectomy[12]. The greatest independent contribution concerning the prediction of 90-day mortality was seen with the American Society of Anesthesiologists (ASA) physical status classification (classes 3-4 versus 1-2: hazard ratio 7.98, 95% confidence interval 3.54-18.01, p<0.0001). In the longer term, for the prediction of later than 90-days mortality, countable diseases such as angina pectoris (Canadian Cardiovascular Society classification of angina pectoris classes 2-4 versus 0-1), and conditions contributing to the Charlson score 2+versus 0-1 were of greater importance[12].

Radical prostatectomy

The latest guidelines of the European Association of Urology (EAU) for prostate cancer (PCa) in 2020, based on the findings of the International Society of Geriatric Oncology (SIOG) Prostate Cancer Working Group, recommend that treatment for senior adults should be based on a systematic evaluation of their health status using the G8 (Geriatric 8)

screening tool[13-15]. Healthy patients with a G8 score >14, or vulnerable patients with reversible impairment after resolution of their geriatric problems, should receive the same treatment as younger patients. Frail patients with irreversible impairment should receive adapted treatment. Patients who are too ill should receive only palliative treatment[13-14]. Patients with a G8 score <14 should undergo a full geriatric evaluation as this score is associated with 3-year mortality. Assessment should include comorbidity, nutritional status and cognitive and physical functions, to determine if the impairment is reversible[13-14].

Comorbidities of a patient can be measured mainly with the Cumulative Illness Score Rating-Geriatrics (CISR-G)[16] and Charlson Comorbidity Index (CCI)[17]. Cognitive impairment can be measured using mini-COG[18], which assesses if the patient is able to make an informed decision[14]. Physical function can be assessed with Karnofsky score[19] and ECOG scores[20]. Nutritional status can be estimated either with the extent of weight loss in the previous 3 months, or with the decline in food intake. In general, a life expectancy of >10 years has been used as the most important condition to consider local treatment for prostate cancer beneficial for a patient[14].

Radical nephroureterectomy

In patients with non-metastatic upper urinary tract carcinoma, treated with radical nephroureterectomy (RNU), preoperative frailty has been associated with higher short-term postoperative complications, as well as longer length of stay (LOS) and higher total hospital charges (THCs)[21].

The Johns Hopkins frailty-indicator was used to stratify patients according to frailty status in a study that included 11 258 RNU patients from the National Inpatient Sample (NIS) database (2000-2015). Frail patients exhibited significantly higher rates of overall complications (62.6% vs 50.9%), in-hospital mortality (1.6% vs 1.0%), non-home-based discharge (22.7% vs 12.1%), longer length of stay (LOS) (6 vs 1 day) and higher THCs ($49 539 vs $39 644)[21]. The Johns Hopkins frailty-indicator includes five phenotypic criteria: unintentional weight loss, exhaustion, low energy expenditure, low grip strength, and/or slowed walking speed[21].

Partial nephrectomy

A single postoperative complications prediction index cannot always evaluate surgical outcomes accurately in complex patient populations. In patients undergoing partial nephrectomy for renal cell carcinoma (RCC), the American College of Surgeons NSQIP Surgical Risk Calculator showed significant discrepancies among observed and predicted outcomes[22]. Additional analyses confirmed these differences remained significant irrespective of surgical approach. Clinically significant underestimations occurred with rates of overall complications, while overestimating minimally invasive partial nephrectomy (MIPN) severe complications[22].

These results emphasize the need for establishing urologic oncology-specific calculators to better predict surgical outcomes for patients undergoing major urologic oncology operations. Alternatively, it is necessary to use a combination of calculators and indexes that take into consideration, not only the age of the patient, but also the comorbidities, the nutritional and cognitive status and the physical function[14,22].

Assessment and optimization of preoperative frailty and prediction of postoperative complications

A review by Michalik C et al. in March 2020 used the variables of the Comprehensive Geriatric Assessment (CGA) and showed that they were, both prospectively and retrospectively, significant predictors of complications of urological surgery. The CGA calculates functional status (FS), fatigue, comorbidity, cognition, mental health, social support, nutrition and geriatric syndromes (e.g. dementia, delirium, falls, incontinence, osteoporosis or spontaneous fractures, neglect or abuse, failure to thrive, constipation, polypharmacy, pressure ulcers, and sarcopenia)[6,23].

Although the use of CGA is not a standard practice in every day urological clinical practice, components of the CGA appear to be predictive of post operative complications. A detailed full CGA is not necessary in all patients, since it requires experience and it is time consuming. However, a variety of screening tests may be useful (e.g. Geriatric 8) in identifying patients requiring complete CGA.

The authors concluded that if it is known much earlier that a major oncological urological procedure is necessary, the optimal time for geriatric evaluation appears to be about 4 weeks before admission, which would allow for intervention or delayed surgery with a clear understanding of the planned procedure and associated risks[6].

Suskind et al. using data from the NSQIP from 2007 to 2013, identified 95,108 patients aged ≥40 years that underwent common urological procedures appearing in the registry more than 1,000 times. Frailty was measured using the NSQIP frailty index[7]. The majority of patients (67.8%) undergoing surgery were aged ≥61 years. The rate of complications increased with increased frailty index (adjusted OR=1.74; 95% CI=1.64-1.85) regardless of the patient's age. The average frequency of complications was 11.7%, with the most common complications being readmission (6.2%), blood transfusion (4.6%) and urinary tract infection (3.1%)[7].

Optimization of the individual parameters of preoperative frailty can improve the surgical outcomes. In order to deliver this aim, it is necessary to include a preoperative risk stratification using a frailty index, for example the ASA score, and cardiopulmonary exercise testing for patients undergoing intra-abdominal surgery, preoperative management of iron deficiency and anemia, and preoperative exercise intervention. Most studies come to the conclusion

that further proof is needed of the utility and validity for improving surgical outcomes through advances in preoperative care[8,24].

Other studies suggest the stratification of patients with the use of multidimensional instruments and parameters before major operations such as radical cystectomy, in order to minimize postoperative complications. Psutka et al (2018), suggest that novel metrics including standardized assessments of dependency, comorbidity severity, sarcopenia, malnutrition, physical and cognitive frailty, and comprehensive geriatric assessments may offer more precise estimates of physiologic age and relative vulnerability to adverse outcomes following radical cystectomy (RC)[25]. The authors claim that the use of standardized multidimensional instruments should be encouraged for patients undergoing consideration for RC to identify potentially modifiable risk factors that can be targeted with prehabilitation interventions[25].

For instance, sarcopenia represents a modifiable risk factor. It has been demonstrated that programs to recover muscle loss decrease length of stay, as well as payer and hospital costs following surgery[25,26].

Furthermore, malnutrition is another potentially modifiable risk factor. Preoperative nutritional interventions such as immunonutrition supplements are associated with lower rates of postoperative complications and may mitigate some of the postoperative inflammatory response following operations such as radical cystectomy[27,28].

Therefore, inclusion of geriatric assessment as part of routine preoperative care and stratification of frailty using a multidisciplinary approach should be considered in all urology patients[8,25].

Conclusion

Frailty is a crucial patient characteristic that affects the surgical outcome of all urologic oncology operations. The use of indexes and calculators to evaluate the health status of every patient before these surgical procedures can assist physicians to choose the most suitable and safe treatment for every individual. Also, it can guide them to alter and improve some of the specific factors that contribute to the frailty of these patients, so that they can safely receive invasive treatment with curative intent.

There is an increasing need for the establishment of widely accepted specific urologic oncology calculators to predict the association between frailty and postoperative complications. However, due to the current lack of such specific indexes the use of a combination of the most accurate calculators is recommended to predict and prevent postoperative complications associated with frailty[9,14,21-22].

References

1. Sathyan S, Verghese J. Genetics of frailty: a longevity perspective. Transl Res 2020 pii: S1931-5244(20)30042-6.
2. Pilotto A, Custodero C, Maggi S, Polidori MC, Veronese N, Ferrucci L. A multidimensional approach to frailty in older people. Ageing Res Rev 2020; 60:101047.
3. Angulo J, El Assar M, Álvarez-Bustos A, Rodríguez-Mañas L. Physical activity and exercise: Strategies to manage frailty. Redox Biol 2020; 20:101513.
4. Wleklik M, Uchmanowicz I, Jankowska EA, Vitale C, Lisiak M, Drozd M, et al. Multidimensional Approach to Frailty. Front Psychol 2020; 11:564.
5. Taylor BL, Xia L, Guzzo TJ, Scherr DS, Hu JC. Frailty and Greater Health Care Resource Utilization Following Major Urologic Oncology Surgery. Eur Urol Oncol 2019; 2(1):21-27.
6. Michalik C, Juszczak K, Maciukiewicz P, Drewa T, Kenig J. Geriatric assessment among elderly patients undergoing urological surgery: A systematic literature review. Adv Clin Exp Med 2020; 29(3):399-407.
7. Suskind AM, Walter LC, Jin C, Boscardin J, Sen S, Cooperberg MR, et al. The Impact of frailty on complications in patients undergoing common urologic procedures: A study from the American College of Surgeons National Surgical Quality Improvement Database. BJU Int 2016; 117(5):836-842.
8. Cui HW, Turney BW, Griffiths J. The Preoperative Assessment and Optimization of Patients Undergoing Major Urological Surgery. Curr Urol Rep 2017; 18(7):54.
9. Sathianathen NJ, Jarosek S, Lawrentschuk N, Bolton D, Konety BR. A Simplified Frailty Index to Predict Outcomes After Radical Cystectomy. Eur Urol Focus 2019; 5(4):658-663.
10. ACS Risk Calculator - Home Page [Internet]. 2020 [cited 2020 June 11]. Available from: https://riskcalculator.facs.org/RiskCalculator/.
11. Daabiss M. American Society of Anaesthesiologists physical status classification. Indian J Anaesth 2011;55(2):111-115.
12. Froehner M, Koch R, Heberling U, Hübler M, Novotny V, Borkowetz A, et al. Which comorbidity classification is best suited to identify patients at risk for 90-day and long-term non-bladder cancer mortality after radical cystectomy? World J Urol 2020; 38(3):695-702.
13. Boyle HJ, Alibhai S, Decoster L, Efstathiou E, Fizazi K, Mottet N, et al. Updated recommendations of the International Society of Geriatric Oncology on prostate cancer management in older patients. Eur J Cancer 2019; 116:116-136.
14. EAU Guidelines. Edn. presented at the EAU Annual Congress Amsterdam 2020. ISBN 978-94-92671-07-3.
15. Bellera CA, Rainfray M, Mathoulin-Pélissier S, Mertens C, Delva F, Fonck M, et al. Screening older cancer patients: first evaluation of the G-8 geriatric screening tool. Ann Oncol 2012;23(8):2166-2172.
16. Parmelee PA, Thuras PD, Katz IR, Lawton MP. Validation of the Cumulative Illness Rating Scale in a geriatric residential population. J Am Geriatr Soc 1995;43(2):130-137.
17. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40(5):373-383.
18. Mini-Cog© - Screening For Cognitive Impairment In Older Adults [Internet]. 2020 [cited 2020 June 11]. Available from: https://mini-cog.com.
19. Karnofsky DA, Abelmann WH, Craver LF, Burchenal JH. The Use of the Nitrogen Mustards in the Palliative Treatment of Carcinoma - with Particular Reference to Bronchogenic Carcinoma. Cancer 1948;1(4):634-56.
20. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol 1982;5(6):649-655.
21. Rosiello G, Palumbo C, Deuker M, Stolzenbach LF, Tian Z, Larcher A, et al. Preoperative frailty predicts adverse short-term postoperative

outcomes in patients treated with radical nephroureterectomy. J Surg Oncol 2020; 121(4):688-696.
22. Blair BM, Lehman EB, Jafri SM, Kaag MG, Raman JD. Predicted versus observed 30-day perioperative outcomes using the ACS NSQIP surgical risk calculator in patients undergoing partial nephrectomy for renal cell carcinoma. Int Urol Nephrol 2018; 50(7):1249-1256.
23. International Society of Geriatric Oncology consensus on geriatric assessment in older patients with cancer. Wildiers H, Heeren P et al. J Clin Oncol 2014; 32: 2595-2603.
24. Mistry PK, Gaunay GS, Hoenig DM. Prediction of surgical complications in the elderly: Can we improve outcomes? Asian J Urol 2017; 4(1):44-49.
25. Psutka SP, Barocas DA, Catto JWF, Gore JL, Lee CT, Morgan TM, et al. Staging the Host: Personalizing Risk Assessment for Radical Cystectomy Patients. Eur Urol Oncol 2018; 1(4):292-304.
26. Friedman J, Lussiez A, Sullivan J, Wang S, Englesbe M. Implications of sarcopenia in major surgery. Nutr Clin Pract 2015; 30:175-9.
27. Hamilton-Reeves JM, Stanley A, Bechtel MD, Yankee TM, Chalise P, Hand LK, et al. Perioperative immunonutrition modulates inflammatory response after radical cystectomy: results of a pilot randomized controlled clinical trial. J Urol 2018; 200:292-301.
28. Hamilton-Reeves JM, Bechtel MD, Hand LK, Schleper A, Yankee TM, Chalise P, et al. Effects of immunonutrition for cystectomy on immune response and infection rates: a pilot randomized controlled clinical trial. Eur Urol 2016; 69:389-92.