ARTICLE IN PRESS

Journal of Geriatric Oncology xxx (xxxx) xxx

FISEVIER

Contents lists available at ScienceDirect

Journal of Geriatric Oncology

journal homepage: www.elsevier.com/locate/jgo



Research Letter to Editor

Pre-operative geriatric screening and assessment as predictors of postoperative complications in older adults with gynecologic cancer: A pilot cohort study on a neglected issue

Filippo Cioli Puviani ^{a,1,*}, Pietro Calogero ^a, Giampaolo Bianchi ^b, Pierandrea De Benedetti ^c, Safia Boussedra ^c, Giulia Dondi ^{c,d}, Anna Myriam Perrone ^{c,d}, Pierandrea De Iaco ^{c,d}, Caterina Galetti ^{a,1}

- ^a Unit of Geriatrics, Department of Medical and Surgical Sciences, IRCCS Azienda Ospedaliero-Universitaria Di Bologna, Bologna, Italy
- b Unit of Internal Medicine, Department of Medical and Surgical Sciences, IRCCS Azienda Ospedaliero-Universitaria Di Bologna, Bologna, Italy
- ^c Division of Oncologic Gynecology, IRCCS Azienda Ospedaliero- Universitaria Di Bologna, Bologna, Italy
- d Centro Di Studio e Ricerca Delle Neoplasie Ginecologiche (CSR), University of Bologna, Bologna, Italy

1. Introduction

As the world population ages, the incidence of gynecologic cancer in older adults is increasing more rapidly than in younger patients [1]. Surgery is the cornerstone of gynecologic cancer treatment, but little is known about optimal therapy in older adults. Preoperative assessment of older patients is challenging not only due to cancer related factors, but also because comorbidity, functional status, social network and geriatric syndromes could play a role in determining the final outcome. Comprehensive Geriatric Assessment (CGA) is a multidimensional evaluation of patients' global health status and consists of validated scales to identify impairments in geriatric domains. In different Geriatric Oncology (GO) settings, it has proved to be useful in identifying and managing underlying undetected medical, functional, and psycho-social impairments that may interfere with treatment [2].

In *IRCSS Policlinico di Sant'Orsola* University Hospital of Bologna (Italy), a collaborative program involving oncologic gynecologists and a geriatrician trained in GO has been in place since 2015. The main purpose is to develop a GO collaborative care intervention to enhance the quality of life, symptom burden, and functional outcomes in patients over 65 years old with gynecologic cancer. CGA is performed not only to help decide on a final cancer treatment plan, but also to provide a geriatric intervention plan for overall patient management before and during treatment. In the present study, we evaluated the associations of pre- and intra-operative variables including CGA with surgical complications in older patients who participated in our pilot GO program and underwent a surgical treatment for gynecologic cancer.

 $\hbox{\it E-mail address: filippociolipuviani@studio.unibo.it (F.~Cioli~Puviani).}$

https://doi.org/10.1016/j.jgo.2022.101419

Received 1 December 2021; Received in revised form 2 December 2022; Accepted 19 December 2022 Available online 18 January 2023 1879-4068/© 2023 Elsevier Ltd. All rights reserved.

2. Material and Method

2.1. Patient Criteria and CGA Interview

From February 2015 to February 2020, we screened a total of 100 consecutive patients referred for CGA by gynecologic oncologists in Bologna University Hospital for eligibility. Inclusion criteria were: age >65 years, a gynecologic cancer diagnosis other than breast and vulvarvaginal cancer, elective surgery, and signed informed consent. Exclusion criteria were: benign or borderline neoplasia at pathology diagnosis and final cancer treatment plan not including surgery. A total of 55 patients were included for the present analysis.

For all patients referred to CGA, a Geriatric 8 (G8) score was calculated by gynecologic oncologists. The G8 is a screening tool that includes seven items from the MiniNutritional Assessment (MNA) and age, with final scores ranging from 0 to 17, and \leq 14 indicating a geriatric risk profile [3]. CGA was performed by a single geriatrician, trained in GO, to eliminate interoperative variability. A validated Italian version of each instrument in CGA was used in patient interview. Corresponding cut-offs were chosen according to previous studies.

Functional status was assessed by Katz Activities of Daily Living scale (ADL) [4], Lawton Instrumental Activities of Daily Living scale (IADL) [5], Eastern Cooperative Oncology Group Scale for Performance Status (PF) [6] and Timed Up and Go (TUG) test [7]. We chose the Cumulative Illness Rating Scale-Geriatric (CIRS-G) to assess comorbidity [8]. Polypharmacy was defined as taking five or more medications for 90 days or more. Nutrition was assessed with the MNA [9]. All patients underwent

 $^{^{\}ast}$ Corresponding author.

¹ These authors contributed equally to this work.

F. Cioli Puviani et al.

Mini Mental State Examination (MMSE) as cognitive impairment screening tool [10]. A short form of Geriatric Depression Scale, Mini-Geriatric Depression Scale (Mini-GDS), was used to screen for depression symptoms [11]. We asked whether patients lived alone as a social support indicator.

2.2. Postoperative Data Collection

After CGA, a multidisciplinary meeting was held for discussion of each patient's treatment plan and, in case of elective surgery, preoperative anesthesia consultation was performed. An anesthesiologist assessed patient's physical health status according to American Society of Anesthesiologists (ASA) classification [12]. All patients underwent a 30-day postsurgical clinical examination by a gynecologic oncologist. Length of operation, procedures performed, residual disease, and 30-day postoperative complications (POCs) were recorded by a gynecologic oncologist. We used the Surgical Complexity Scoring (SCS) system validated by Aletti et al. in gynecologic oncology: scores ranging from 1 to 3 were assigned to each surgical procedure based on its complexity [13]. A POC was defined as any event occurring within 30 days of surgery, and was graded according to Clavien-Dindo classification [14]. Due to possible report bias of grade one complications, we only considered grade 2 or higher complications as outcome variables. All outcomes were entered into a password-protected database and reviewed by a gynecologic oncology team physician.

2.3. Data Analysis

Statistical analysis was performed using SPSS for Windows v.25 (SPSS Inc., Chicago, IL, USA). Continuous variables were reported using mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. Absolute prevalence and percentage were used for categorical variables. Univariate analyses were performed to test the significance of each variable in relation to the outcome, using the chi square test or Fisher's exact test for dichotomous variables and the Mann–Whitney \boldsymbol{U} test for continuous variables. Factors associated with the outcome were identified using multivariate logistic regression and results were summarized with odds ratios (ORs) along with a 95% confidence interval (95%CI). \boldsymbol{P} values <0.05 were considered statistically significant.

3. Results

3.1. Baseline Characteristics

A total of 55 patients (55% of those referred to CGA) were included. The most represented age group was 70–74 years (21 patients, 38.2%). All patients had a primary gynecologic cancer: 26 epithelial ovarian cancers, one squamous cell carcinoma of the cervix, 26 endometrial cancers, and two uterine sarcomas. Thirty-four interventions could be considered as primary surgery and in 46 cases cytoreduction was complete. Only three interventions had macroscopic residual tumour at primary cancer site and all endometrial cancer surgeries were R0 (a microscopically margin-negative resection). Twenty patients had laparoscopic surgery, five patients had robotic surgery; 14 (25.4%) patients had intermediate or high complexity surgery. Median hospital stay was five days and only four patients were discharged from our hospital after ten days.

Our population had a good geriatric profile: only 27 (49.1%) patients had a G8 score $\leq 14,\,94.5\%$ and 90.9% were independent in ADL and IADL, respectively, 67,3% completed TUG in less than 10 seconds, 23.6% were living alone, 29.1% had at least one severe comorbidity in addition to cancer, median number of comorbidities was 4, polypharmacy was present in 23.6% of patients, depression screening was positive for 23.6% of patients, only 9.1% tested positive for cognitive impairment, and nutritional assessment identified risk of malnutrition in

40% of patients. Pre-anesthesia assessment resulted in 58.7% patients classified as ASA 3 and none as ASA 1.

3.2. Postoperative Complications

We recorded postoperative complications rated greater than grade 2 on the Clavien-Dindo classification for 16 patients (29.1%). Most of these events were graded as minor. In univariate analysis, only G8 was significantly associated with POCs. Both age and SCS, treated as quantitative variables, did not reach statistical significance. Among CGA and oncological/surgical variables, only G8, polypharmacy, laparotomy, and cancer type were selected to be tested in multiple logistic regression analysis to adjust for multiple risk factors. In a multivariable logistic model adjusted for age and surgical complexity, the only variable found to be independently associated with POCs was G8(Table 1).

4. Discussion

To the best of our knowledge, only one previous study has examined the predictive value of CGA components in gynecologic cancer surgery [15]. It was a prospective study of 60 consecutive patients ≥70 years of age admitted to Seoul National University Hospital for elective surgery in gynecologic cancer treatment. Interviews for CGA were conducted one or two days prior to surgery by a gynecologic oncologist with training in geriatrics. The study included low complexity procedures such as vaginal hysterectomy and vulvar wide excision; only one laparoscopy surgery was performed. Surgical complexity was the only independent POCs predictor, including any POC and those of grade 2 or higher.

One of the strengths of our pilot GO program was the crosstalk between geriatrician and gynecologic oncology team; CGA results were interpreted in relation to cancer treatment and geriatric intervention plan. Patients were selected after discussion between geriatrician and surgeon, so treatment was carefully considered and a population with a good geriatric profile underwent surgery. This may explain the fact that most of the patients who received surgery were rather fit and that CGA variables were not related to complications. A relevant number of patients underwent complex surgery and optimal cytoreduction, regardless of multiple surgical risk factors. Unlike the study by Suh and al., almost half of patients had laparoscopic or robotic surgeries. In terms of study limitations, the small sample size and the low rate of POCs has lowered the statistical power of the results and, since it is single institution study, postoperative outcomes could have been influenced by the skills and quality of surgeons and medical staff. Moreover, we included only patients referred for CGA by gynecologists, thus missing patients over 65 years of age who underwent surgery without a preoperative CGA, leading to possible selection bias.

This is a prospective explorative study on CGA predictive value in a neglected setting, such as gynecologic cancer surgery in older adults. Our findings suggest that the G8 screening tool could be also a 30-day POCs predictor. Larger and multicenter studies are needed to confirm

Table 1Multivariate analysis of the association between components of CGA and surgical complications adjusted for age and surgical Complexity Score.

CGA components and other characteristics	Any complication			
	OR	95%CI	p	
G8 ≤ 14	4.80	1.30-17.66	0.018	
Age	1.10	0.96 - 1.26	0.155	
≥ 5 medications	2.78	0.69-11.16	0.209	
Open surgery (or converted to open surgery)	2.99	0.72 - 12.48	0.229	
Surgical Complexity Score	1.10	0.78 - 1.55	0.434	
Ovarian cancer	1.02	0.22-4.70	0.697	

Abbreviations: CGA = comprehensive geriatric assessment, $OR = odds \ ratio$, CI = confidence interval, G8 = geriatric 8.

ARTICLE IN PRESS

F. Cioli Puviani et al.

Journal of Geriatric Oncology xxx (xxxx) xxx

these results and to focus on post-surgery quality of life and functional status.

Funding information

LOTO Onlus is a Non-Profit Organization aiming at improving research and awareness about ovarian cancer in Italy and supported our GO project.

Authors contribution

Conceptualization and Methodology: C. Galetti, F. Cioli Puviani. Investigation: C. Galetti, F. Cioli Puviani, P. De Benedetti Data Curation F. Cioli Puviani, P. De Benedetti, S. Boussedra. Formal analysis: G. Bianchi, F. Cioli Puviani Writing - Original Draft: C. Galetti, F. Cioli Puviani.

Writing - Review & Editing Caterina Galetti, F. Cioli Puviani, Pierandrea De Benedetti, Safia Boussedra, Giulia Dondi, Anna Myriam Perrone, Pierandrea De Iaco, Pietro Calogero, Giampaolo Bianchi

Declaration of Competing Interest

The authors declare that there are no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://data.mendelev.com/datasets/jpdch96s95.

References

 Dumas L, et al. Improving outcomes for older women with gynaecological malignancies. Cancer Treat Rev 2016;50:99–108. https://doi.org/10.1016/j. attr. 2016.08.007

- [2] Maas HAAM, Janssen-Heijnen MLG, Olde Rikkert MGM, Machteld Wymenga AN. Comprehensive geriatric assessment and its clinical impact in oncology. Eur J Cancer Oxf Engl 2007;1990(43):2161–9. https://doi.org/10.1016/j. aica.2007.09.002
- [3] Soubeyran P, et al. Screening for vulnerability in older cancer patients: the ONCODAGE prospective multicenter cohort study. PLoS One 2014;9:e115060. https://doi.org/10.1371/journal.pone.0115060.
- [4] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963;185:914–9. https://doi.org/10.1001/ jama.1963.03060120024016.
- [5] Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179–86.
- [6] Oken MM, et al. Toxicity and response criteria of the eastern cooperative oncology group. Am J Clin Oncol 1982;5:649–55.
- [7] Huisman MG, et al. 'Timed up & go': a screening tool for predicting 30-day morbidity in onco-geriatric surgical patients? A Multicenter Cohort Study. PLoS One 2014;9:e0086863. https://doi.org/10.1371/journal.pone.0086863.
- [8] Miller MD, et al. Rating chronic medical illness burden in geropsychiatric practice and research: application of the cumulative illness rating scale. Psychiatry Res 1992;41:237–48. https://doi.org/10.1016/0165-1781(92)90005-n.
- [9] Guigoz Y. Mini nutritional assessment: a practical assessment tool for grading the nutritional state of elderly patients. Facts Res Geyontol 1994;4:15–59.
- [10] Folstein MF, Folstein SE, McHugh PR. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12: 189–98. https://doi.org/10.1016/0022-3956(75)90026-6.
- [11] Rinaldi P, et al. Validation of the five-item geriatric depression scale in elderly subjects in three different settings. J Am Geriatr Soc 2003;51:694–8. https://doi. org/10.1034/j.1600-0579.2003.00216.x.
- [12] Keats AS. The ASA classification of physical status a recapitulation. Anesthesiology 1978;49:233–6. https://doi.org/10.1097/00000542-197810000-00001.
- [13] Aletti GD, Dowdy SC, Podratz KC, Cliby WA. Relationship among surgical complexity, short-term morbidity, and overall survival in primary surgery for advanced ovarian cancer. Am J Obstet Gynecol 2007;197(676):e1–676.e7. https:// doi.org/10.1016/j.ajog.2007.10.495.
- [14] Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205–13. https://doi.org/10.1097/01.sla.0000133083.54934.ae.
- [15] Suh DH, et al. Pre- and intra-operative variables associated with surgical complications in elderly patients with gynecologic cancer: the clinical value of comprehensive geriatric assessment. J Geriatr Oncol 2014;5:315–22. https://doi. org/10.1016/j.jgo.2014.03.004.