International Journal of Gerontology 15 (2021) 12–15
https://doi.org/10.6890/IJGE.202101_15(1).0003

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

# A Pilot Study to Examine the Feasibility of Personalizing Treatment Options of Elderly Breast Cancer Patients through Individual Risk Profiling

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ARTICLE INFO

Accepted 24 August 2020

*Keywords:*
breast cancer,
comprehensive geriatric assessment,
elderly,
risk profiling,
pilot

SUMMARY

*Background:* Decision for the best optimal treatment for the elderly is always a challenge, in particular when deciding for surgery. Studies have showed for frail elderly with limited life expectancy, primary endocrine therapy alone may be appropriate with equivalent survival. Those patients with longer life expectancy could have survival gain from surgery. A comprehensive geriatric assessment (CGA) would be useful to predict the survival probability and guide the optimal treatment.
*Methods:* Consecutive new patients aged 70 or above with a diagnosis of stage I to III breast cancer, were recruited from July to December 2017. The decision of treatment was independently made regardless of the study assessment. A prospective cross-sectional study using CGA was conducted. Scoring for each component of CGA was measured and the correlation with the treatment was analysed.
*Results:* Twenty-four patients were recruited during the study period. Nineteen of them received surgical treatment whereas five received non-surgical treatment. Older age ($p = 0.010$), higher Eastern Cooperative Oncology Group (ECOG) score ($p = 0.028$), higher degree of dependence by the instrumental activities of daily living ($p = 0.018$), cognitive impairment by the Hong Kong version of montreal cognitive assessment (HK-MoCA) ($p = 0.006$), and very high Charlson comorbidity index (> 5) ($p = 0.047$) were significantly related to non-surgical treatment.
*Conclusion:* This pilot study confirmed the feasibility in conducting CGA to personalize treatment options for older breast cancer patients. A larger prospective trial is ongoing to validate the impact of each CGA domain in relation to the treatment outcome.



## 1. Introduction

In Hong Kong, breast cancer is the most common cancer in women. The Hong Kong Cancer Registry in 2017[1] reported an annual incidence of 4,373, and breast cancer accounted for 27.0% of all female cancer diagnosed in Hong Kong. Among these new cases in 2017, 793 patients (18.1%) were aged 70 or above. A gradually increasing trend of breast cancer patients diagnosed with increasing age was also observed. In addition, the latest Hong Kong Population Projections 2017–2066 stated that the proportion of older population over the age of 70 was expected to increase from 10.5% to 16.5% in the next ten years.[2] As a result, we should also expect an increase in the incidence of older patients with breast cancer in Hong Kong.

Deciding on the optimal treatment for an older patient with breast cancer is a real challenge.[3] Surgery still remains the mainstay for the treatment of operable breast cancer, yet it is associated with comparatively high postoperative morbidities and mortalities in elderly patients. An avoidable operation not only can result in potential complications and increase suffering of the elderly, but also will incur healthcare burden and hospital costs. Historically primary hormonal therapy (PHT) with Tamoxifen is considered as an alternative to surgery for estrogen receptor positive breast cancer.[4]

A systemic review of randomized controlled trials and cohort studies comparing surgery versus PHT for older patients with operable breast cancer showed that surgery was more advantageous over PHT in the matter of disease control, and there was a possibly survival benefit in patients with longer life expectancy of more than five years.[5] The guidelines of the International Society of Geriatric Oncology (SIOG) also recommended that PHT may be considered in patients who refused surgery, with a short life expectancy less than two years, or considered not fit for surgery.[6]

The prediction of life expectancy is complicated. A comprehensive geriatric assessment (CGA) has been developed as a quantitative measure of an elderly's physical and psychosocial status. It composes of various domains including comorbidity, functional ability, cognition, emotional state, and nutritional condition. A CGA is regarded as an objective method to predict the estimated lifespan among older adults. The SIOG[6] and the National Comprehensive Cancer Network[7] have recommended the incorporation of geriatric assessment in treatment planning.

A number of studies have investigated various domains within CGA to identify the variables with significant impact on outcome or survival.[8] Most of the researches were conducted in the Western countries. Due to biological and cultural difference,[9] we would like to investigate whether the concept of CGA is applicable in Chinese population.

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This study serves as a pilot to test the practicability of applying CGA in Chinese cohort and the correlation with the treatment options.

## 2. Patients and methods

Patients aged 70 or above who were diagnosed with Stage I to III breast cancer and received treatment at Tung Wah Hospital Breast Centre, a Hong Kong University affiliated academic breast unit serving the population in Hong Kong West Cluster, and as a local tertiary referral centre, were recruited to the study.

Patients with evidence of metastatic disease, or patients who failed to give informed study consent were excluded.

Within six weeks after the diagnosis of breast cancer, patients were asked to fill in a CGA questionnaire, which consisted of the following eight distinct domains:

1. Functional status
   i. Eastern Cooperative Oncology Group (ECOG) performance status:[10] grade 0 to 4, where grade 0 indicates fully active and grade 4 indicates completely disabled.
   ii. Barthel Index of Activities of Daily Living[11] (BI): score 0 to 20, includes ten variables in basic personal activities such as bathing, feeding and continence.
   iii. Instrumental Activities of Daily Living[12] (IADL): score 0 to 8, determines function in activities such as shopping, cleaning and cooking.
2. Cognitive function – Hong Kong version of Montreal Cognitive Assessment (HK-MoCA).[13]
3. Emotional condition – Geriatric Depression Scale (GDS) Short Form 15.[14]
4. Nutrition status – Body mass index (BMI).
5. Comorbidity – Charlson comorbidity index.[15] A list of comorbid conditions is classified into classes and weighted a score of 1, 2, 3, or 6.
6. Anesthetic assessment – American Society of Anesthesiologists (ASA) grade.[16]
7. Pharmacy: number of medications.
8. Geriatric syndromes:[17] includes delirium, dementia, depression, failure to thrive, falls, incontinence, neglect and abuse, and osteoporosis.

Clinical parameters including age, sex, stage of disease and type of treatment were obtained for each patient. Decision of the primary treatment was drawn by the multi-disciplinary team including breast surgeons and oncologists, and independently made regardless of the study assessment.

Continuous data were presented as mean (± standard deviation). Comparison between the groups was made by the Wilcoxon rank-sum test or Fisher's exact test when appropriate. All analyses were performed using SPSS version 24.

Ethical approval for the present study was obtained from the Institutional Review Board (IRB) of the University of Hong Kong / Hospital Authority Hong Kong West Cluster in August 2017 (IRB Reference Number: UW 17-291).

## 3. Results

Consecutive twenty-four patients aged 70 or above fulfilling the inclusion criteria and received treatment from August to December 2017 were recruited into this prospective pilot study.

The participation uptake rate of the study was 100%. The mean duration to complete the CGA questionnaire was 36.5 minutes (range 25–60 minutes).

Nineteen patients received surgical treatment and five had non-surgical treatment. Four patients had endocrine therapy as the primary treatment and one patient was treated with primary radiotherapy. The mean age of patients was 77 years with a maximum age of 95 years. Patients received non-surgical treatment (mean age 86 years) were significantly older than those received surgical treatment (mean age 75 years) (p = 0.010).

Table 1 showed the comparison of clinical parameters between the surgical and non-surgical groups. No statistical difference was demonstrated between the two groups in terms of clinical stage of

**Table 1**
Comparison of clinical parameters between the surgical and non-surgical groups.

| | Surgical treatment (n = 19) | Non-surgical treatment (n = 5) | p-value |
|---|---|---|---|
| Mean age at diagnosis (± standard derivation) | 75.05 ± 4.30 | 85.80 ± 8.87 | 0.010 |
| T stage | | | 0.464 |
| T1 | 6 (31.6%) | 1 (20.0%) | |
| T2 | 12 (63.2%) | 3 (60.0%) | |
| T3 | 0 (0.0%) | 1 (20.0%) | |
| T4 | 1 (5.3%) | 0 (0.0%) | |
| N stage | | | 0.311 |
| N0 | 9 (47.4%) | 5 (100.0%) | |
| N1 | 7 (36.8%) | 0 (0.0%) | |
| N2 | 1 (5.3%) | 0 (0.0%) | |
| N3 | 2 (5.9%) | 0 (0.0%) | |
| Histology | | | 1.000 |
| IDC | 18 (94.7%) | 5 (100.0%) | |
| ILC | 1 (5.3%) | 0 (0.0%) | |
| ER | | | 0.521 |
| Positive | 17 (89.5%) | 4 (80.0%) | |
| Negative | 2 (10.5%) | 1 (20.0%) | |
| PR | | | 0.521 |
| Positive | 17 (89.5%) | 4 (80.0%) | |
| Negative | 2 (10.5%) | 1 (20.0%) | |
| HER2 | | | 0.380 |
| Positive | 1 (5.3%) | 1 (20.0%) | |
| Negative | 18 (94.7%) | 4 (80.0%) | |

The p-values were computed by Wilcoxon rank-sum test or Fisher's exact test when appropriate.
Abbreviations: IDC = invasive ductal carcinoma; ILC = invasive lobular carcinoma; ER = estrogen receptor; PR = progesterone receptor; HER2 = human epidermal growth factor receptor 2.

the disease, histology and immunohistochemical status of the breast tumor.

Associations between CGA and the treatment options was shown in Table 2. The group of patients who received non-surgical treatment had higher ECOG score implying worse functional status. On the report of the IADL, the non-surgical group had higher degree of dependence. As determined by the HK-MoCA, the non-surgical group had more cognitive impairment, and they had very high Charlson comorbidity index as compared to the surgical group.

## 4. Discussion

We had conducted a retrospective study comparing Chinese older patients with breast cancer with their younger counterparts.[18] Patients with breast cancer treated surgically in our breast unit from 2000 to 2015 were recruited. 3,825 patients had surgery during the study period, of which 510 patients (13.3%) were aged 70 and above. We found that older breast cancer patients had worse overall survival than those younger. The 5-year overall survival for patients aged 70 and above was 76.9%, which was significantly poorer than their younger counterparts (89.5%, p = 0.000)

Due to their advanced age, older patients are associated with more comorbidity, which may affect the decision making for treatment[19] as well as the outcome. The assessment of fragility is complex. A comprehensive geriatric assessment (CGA) is an in-depth assessment compiling of severe domains to evaluate an individual's health and provide a framework for personalized treatment plan.[20]

While CGA is the gold standard, its components may vary. In a survey conducted by the Surgical Task Force at SIOG,[21] only 6.4% surgeons used CGA in daily practice. One of the reasons for the low utilization was that a full CGA was sometimes considered delicate and time-consuming.

A number of studies have investigated various domains within CGA to identify the variables with significant impact on outcome or survival.[22] By incorporating the predictive factors, a scoring system or a risk score was developed to predict the survival probability in elderly patients. In a Singaporean study looking at elderly Asian patients, a clinical scoring system was developed based on significant multivariate prognostic factors within CGA.[23] Stotter et al. also created a risk score to estimate the 3-year survival using CGA.[24] Although further validation by prospective trials is needed, these two studies laid the cornerstone for further researches.

With different cultural background and biological makeup,[9] a scoring system dedicated for Chinese elderly patients with breast cancer is prerequisite as an assessment tool for decision making. This present study has proved it is useful to conduct a CGA in a clinical setting for Chinese elderly patients with breast cancer.

The limitation of the study was the small sample size and lack of long term survial data and quality of life assessment, which made it impossible to perform the multivariate analysis to identify the independent significant prognostic factors within the clinical parameters and domains of CGA.

To investigate the independent predictors and formulate a clinician-friendly scoring system from the complex full assessment, we require a larger data set by recruiting more elderly breast cancer patients. With the success of this pilot feasibility study, we are now participating in a multi-centre study including the United Kingdom, and the recruitment is ongoing.

**Table 2**
Comparison of comprehensive geriatric assessment components between the surgical and non-surgical groups.

| | Surgical treatment (n = 19) | Non-surgical treatment (n = 5) | p-value |
|---|---|---|---|
| ECOG | | | 0.028 |
| 0–1 | 15 (78.9%) | 1 (20.0%) | |
| 2–4 | 4 (21.1%) | 4 (80.0%) | |
| BI | | | 0.058 |
| Independence | 14 (73.7%) | 2 (40.0%) | |
| Moderate dependence | 5 (26.3%) | 1 (20.0%) | |
| Severe dependence | 0 (0.0%) | 2 (40.0%) | |
| IADL | | | 0.018 |
| Independence | 18 (94.7%) | 2 (40.0%) | |
| Dependence | 1 (5.3%) | 3 (60.0%) | |
| HK-MoCA | | | 0.006 |
| Normal | 17 (89.5%) | 1 (20.0%) | |
| Abnormal | 2 (10.5%) | 4 (80.0%) | |
| GDS | | | 0.260 |
| Normal | 18 (94.7%) | 2 (66.7%) | |
| Depressed | 1 (5.3%) | 1 (33.3%) | |
| BMI | | | 0.133 |
| Underweight | 0 (0.0%) | 1 (20.0%) | |
| Normal | 5 (26.3%) | 3 (60.0%) | |
| Overweight | 3 (15.8%) | 0 (0.0%) | |
| Obese class I | 7 (36.8%) | 0 (0.0%) | |
| Obese class II | 4 (21.1%) | 1 (20.0%) | |
| Charlson comorbidity index | | | 0.047 |
| High (3–4 points) | 14 (73.7%) | 1 (20.0%) | |
| Very high (≥ 5 points) | 5 (26.3%) | 4 (80.0%) | |
| ASA | | | 1.000 |
| II | 13 (68.4%) | 3 (60.0%) | |
| III | 6 (31.6%) | 2 (40.0%) | |
| Polypharmacy (> 4 medications) | | | 1.000 |
| No | 14 (73.7%) | 4 (80.0%) | |
| Yes | 5 (26.3%) | 1 (20.0%) | |
| Geriatric syndromes | | | 0.078 |
| Presence | 3 (15.8%) | 3 (60.0%) | |
| Absence | 16 (84.2%) | 2 (40.0%) | |

The p-values were computed by Fisher's exact test.
Abbreviations: ECOG = Eastern Cooperative Oncology Group (ECOG) performance status; BI = Barthel Index of Activities of Daily Living; IADL = instrumental activities of daily living; HK-MoCA = Hong Kong version of Montreal Cognitive Assessment; GDS = Geriatric Depression Scale (GDS) Short Form 15; BMI = body mass index; ASA = American Society of Anaesthesiologists grade.

## Acknowledgements

We thank Dr. Joseph Kwan, Dr. Roland Leung and Dr. Annie Chu for their expertise advice in the study design; Ms Rachel Chau and Ms Kelly Chan for conducting the cognitive assessment; Mr Wing Pan Kuk and Mr Ling Hiu Fung for statistical analysis.

## Funding/support statement

There was no specific grant from any funding agency.

## Declaration of any potential financial and non-financial conflicts of interest

There is no potential financial and non-financial conflicts of interest.

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