

## Association of preoperative G8 score with survival, preoperative anemia and vitamin D status in gynecologic cancer patients: 5-year analysis of the Frail-B study

Valerie Catherine Linz <sup>a,\*</sup>, Emma Liebau <sup>a</sup>, Laura Herrmann <sup>a</sup>, Markus Schepers <sup>b</sup>, Katharina Gillen <sup>c</sup>, Michael Mohr <sup>d</sup>, Mona Wanda Schmidt <sup>a</sup>, Marcus Schmidt <sup>a</sup>, Annette Hasenburger <sup>a</sup>

<sup>a</sup> Department of Obstetrics and Gynecology, University Medical Center of the Johannes Gutenberg University Mainz, Langenbeckstraße, 1, 55131 Mainz, Germany

<sup>b</sup> Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI), University Medical Center of Johannes Gutenberg University Mainz, Langenbeckstraße 1, 55131 Mainz, Germany

<sup>c</sup> Department of Gynecology, Diakonie Hospital Jung-Stilling Siegen, Wichernstraße 40, 57074 Siegen, Germany

<sup>d</sup> Geriatric Department, University Medical Center of the Johannes Gutenberg University Mainz, Langenbeckstraße, 1, 55131 Mainz, Germany

### HIGHLIGHTS

- Low G8 score correlated with shorter progression-free survival in gynecologic cancers.
- Surgical resection status was the main predictor of outcome across all gynecological tumor types.
- First link between low vitamin D levels and positive G8 screening results.
- Low G8 scores were associated with reduced or de-escalated adjuvant therapy.
- G8 may identify modifiable risks like anemia or vitamin D deficiency before surgery.

### ARTICLE INFO

#### Article history:

Received 12 November 2025

Received in revised form 30 December 2025

Accepted 4 January 2026

Available online xxx

#### Keywords:

G8 geriatric screening tool

Frailty

Comprehensive geriatric assessment

Gynecologic oncology

Vitamin D

### ABSTRACT

**Objective.** Frailty, nutritional deficiencies, and anemia frequently coexist in gynecologic cancer and may adversely influence clinical outcomes. This study aimed to evaluate the prognostic value of the G8 geriatric screening tool (G8) for survival outcomes in patients undergoing gynecologic oncology surgery, with postoperative complications and selected modifiable preoperative conditions assessed as secondary outcomes.

**Methods.** Patients  $\geq 60$  years undergoing gynecologic oncology surgery were prospectively screened for frailty between May 2020 – June 2025. Survival was evaluated with Kaplan-Meier curves and Cox regression. Propensity score matching included demographics, comorbidities, and tumor characteristics; matched samples were analyzed using weighted Cox models.

**Results.** Of 257 screened patients, 180 were included (endometrial  $n = 72$ , ovarian  $n = 71$ , vulvar  $n = 26$ , cervical  $n = 6$ , vaginal cancer  $n = 5$ ; mean age  $69.6 \pm 7.9$  years; follow-up  $25.1 \pm 16.3$  months). G8 positive patients ( $\leq 14$  points) had more comorbidities and were more likely to present with preoperative anemia, hypoalbuminemia, and vitamin D or B12 deficiency. FIGO stages, surgical approach and postoperative complications were comparable. G8 positive patients were less likely to receive standard adjuvant therapy ( $p = 0.003$ ). In matched analyses, G8 positivity remained significantly associated with reduced progression-free survival (HR: 1.87, 95% CI: 1.01–3.49,  $p = 0.047$ ) and showed a trend toward worse overall survival (HR: 2.25, 95% CI: 0.98–5.16,  $p = 0.055$ ). Surgical resection status was the strongest predictor of oncological outcome.

**Conclusions.** A low preoperative G8 score was associated with reduced progression-free and potentially worse overall survival in older women with gynecologic tumors. The G8 may help identify modifiable factors such as anemia or vitamin D deficiency, while complete tumor resection remained the strongest prognostic factor.

© 2026 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

\* Corresponding author at: Valerie Catherine Linz, Langenbeckstraße 1, 55131 Mainz, Germany.

E-mail address: [Valerie.linz@unimedizin-mainz.de](mailto:Valerie.linz@unimedizin-mainz.de) (V.C. Linz).

## 1. Introduction

Gynecological malignancies are among the most common cancers in women worldwide and predominantly affect older patients. The rising incidence of these tumors coincides with increasing life expectancy, resulting in a growing proportion of older, often multimorbid women facing these diseases. Frailty, characterized by reduced physiological reserve and increased vulnerability to stressors, has emerged as a critical factor influencing treatment tolerance and outcomes in this population [1–3].

In gynecologic oncology, frailty assessment is increasingly recognized as essential for risk stratification and treatment planning. Although comprehensive geriatric assessment is recommended for older cancer patients [4], its routine implementation is often limited by time and resource constraints. There is growing evidence that geriatric assessment can enhance treatment outcomes by patient-individualized treatment modifications such as chemotherapy regimens with lower chemotherapy-related toxicity, surgical approaches with lower complication rates, and interventions improving both functional status and quality of life [5,6]. The G8 geriatric screening tool (G8) is a brief, frailty-specific instrument developed to identify older cancer patients who may benefit from further geriatric assessment and who may be at increased risk for adverse outcomes [7–9]. There is increasing interest in brief and practical screening tools to identify vulnerable patients in the preoperative setting.

Beyond frailty screening, additional factors such as nutritional deficiencies in vitamin D and vitamin B12 are common in older adults and have been associated with frailty, functional impairment, and anemia [10,11]. As potentially modifiable factors, these parameters may help to better capture and describe vulnerability in older gynecologic oncology patients.

Accordingly, the primary objective of this study was to evaluate the prognostic value of the G8 for survival outcomes in patients undergoing gynecologic oncology surgery. Secondary objectives included the assessment of postoperative complications and the association between G8 status and selected modifiable preoperative conditions.

## 2. Material and methods

### 2.1. Data collection and frailty assessment

From May 2020 to June 2025, patients scheduled for gynecologic oncology surgery at the University Medical Center Mainz in Germany were prospectively screened for frailty as part of the ongoing observational Frail-B study investigating frailty in gynecologic oncology patients (<https://drks.de/search/en/trial/DRKS00032361/entails>). The present analysis represents a sub study/ interim analysis and was designed to evaluate the prognostic value of preoperative G8 screening for survival outcomes. Secondary objectives included the assessment of perioperative outcomes, such as postoperative complications, and the association between G8-detected frailty and selected modifiable preoperative conditions, including anemia and vitamin deficiencies. Patients were eligible for inclusion if they met at least one of the following criteria: age  $\geq 60$  years, body mass index (BMI)  $>35$  kg/m<sup>2</sup>, or a clinically frail appearance. The age threshold of  $\geq 60$  years was chosen to capture early manifestations of frailty in multimorbid gynecologic oncology patients, as suggested by prior institutional analyses [12,13]. A BMI  $>35$  kg/m<sup>2</sup> was included based on institutional perioperative risk stratification to identify obesity-associated vulnerability, despite the fact that higher BMI values ( $\geq 23$  kg/m<sup>2</sup>) are scored favorably within the G8 screening tool. Clinical frailty was assessed based on the nurse's preoperative impression, including mobility, muscle mass, gait, and fatigue. Patients with precursor lesions or incomplete follow-up were excluded.

Frailty assessment was performed in two steps: Initial screening included the G8, Lee Schonberg Index, routine blood parameters; hand

grip strength was added from 2023 onward. The components of the G8 geriatric screening tool are shown in Fig. 1. Preoperative physical status was evaluated using the ASA (American Society of Anesthesiologists) Physical Status classification [14] and the ECOG (Eastern Cooperative Oncology Group) performance status [15]. Patients with a positive G8 result (defined as  $\leq 14$  points) underwent further evaluation, including fall history and selected tests from the geriatric assessment. The data of this second screening were still preliminary and will be analyzed at a later stage.

To account for background non-cancer mortality, the Lee Schonberg index was used as a validated prognostic tool for community-dwelling adults aged 50 and older to estimate medium- to long-term all-cause mortality risk based on age, comorbidities, and functional status [16–18]. The Lee Schonberg Index was calculated online with ePrognosis (<https://eprognosis.ucsf.edu/leeschonberg.php>) in the presence of the patient according to the ASCO guidelines recommending using a validated tool listed at ePrognosis to estimate non-cancer-based life expectancy [19]. The 5-year mortality risk for the Schonberg index was used [17,20]. After scoring each comorbidity, the patient's 10-year survival rate was calculated according to the age-adjusted Charlson Comorbidity Index with an online tool (<https://www.mdcalc.com/calc/3917/charlson-comorbidity-index-cci>) [21–23]. Standard-of-care therapy was defined as guideline-concordant treatment based on interdisciplinary tumor board recommendations.

Preoperative anemia was defined as hemoglobin (Hb)  $<12$  g/dL, in accordance with WHO (World Health Organization) criteria for non-pregnant women [24]. Preoperative hemoglobin levels and intra- and postoperative red blood cell transfusions were recorded. Vitamin D and B12 measurements were included from April 2023. Vitamin D

Item	Question / Categories	Score
Food intake	Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	Severe decrease (0) Moderate decrease (1) No decrease (2)
Weight loss	Weight loss during the last 3 months	$>3$ kg (0) Does not know (1) 1–3 kg (2) No weight loss (3)
Mobility	Mobility	Bed or chair bound (0) Able to get out of bed/chair but does not go out (1) Goes out (2)
Neuropsychological problems	Neuropsychological problems	Severe dementia or depression (0) Mild dementia (1) No psychological problems (2)
Body mass index	Body mass index (kg/m <sup>2</sup> )	$<19$ (0) 19– $<21$ (1) 21– $<23$ (2) $\geq 23$ (3)
Polypharmacy	Takes more than three prescription drugs per day?	Yes (0) No (1)
Self-perceived health	Compared with others of the same age, how does the patient rate their health?	Not as good (0) Does not know (0.5) As good (1) Better (2)
Age	Age	$> 85$ years (0) 80–85 years (1) $<80$ years (2)

**Fig. 1.** G8 geriatric screening tool (adapted from Bellera et al.)

The G8 geriatric screening tool as originally described by Bellera et al. A total score  $\leq 14$  indicates frailty and the need for further geriatric assessment [8]. G8: geriatric 8. Reference: Bellera CA, Rainfray M, Mathoulin-Pélissier S, et al. Screening older cancer patients: first evaluation of the G8 geriatric screening tool. *Ann Oncol.* 2012;23: 2166–2172.

sufficiency was defined as serum vitamin D levels  $\geq 30$  ng/mL, with levels between 20 and 29 ng/mL considered insufficient [25]. Vitamin B12 levels below 200 ng/L were classified as deficient [26]. Ethical approval was obtained from the State Medical Association of Rhineland-Palatinate (ID: 16691) as well as written informed consent from the included patients.

## 2.2. Statistical analysis

Descriptive analyses were conducted using IBM (International Business Machines Corporation) SPSS (Statistical Package for the Social Sciences) Statistics 29.0.2.0, while propensity score matching was performed in R version 4.2.3 [27,28]. Categorical variables were summarized as counts and percentages; continuous variables as mean  $\pm$  SD (standard deviation) or median (IQR: interquartile range). Based on distribution, assessed with the Shapiro–Wilk test, group comparisons used the *t*-test or Mann–Whitney *U* test, and categorical data the chi-square test. Several variables reflect overlapping aspects of functional status and comorbidity (e.g. ECOG, ASA, and the Charlson Comorbidity Index). To account for this overlap, we used a stepwise analytical approach combining multivariable Cox regression and propensity score full matching. Cox regression was performed, with variables significant in univariable analysis ( $p < 0.05$ ) entered into a multivariable model via backward stepwise selection. Kaplan–Meier curves estimated progression-free and overall survival. The starting point was the date of surgery, and endpoints were defined as recurrence/ progression, death, or last follow-up. Patients without events or with missing follow-up data were censored. Progression-free survival endpoint included locoregional recurrences, disease progression, distant metastases, and death from any cause. Hazard ratios (HR) with corresponding 95% confidence intervals (CI) were calculated. Survival curves were compared using the log-rank test. All statistical tests were two-sided, and a *p*-value below 0.05 was considered statistically significant. No adjustment for multiple comparisons was made; results should therefore be interpreted as exploratory. To address baseline imbalances between the G8 positive and G8 negative groups, we used propensity score matching. A propensity score for each patient was estimated using a logistic regression model with G8 status (positive vs. negative) as the dependent variable and the following baseline characteristics as independent variables: ECOG performance status, ASA physical status, surgical resection status, FIGO stage, age-adjusted Charlson Comorbidity Index, age at surgery, and BMI. Full-matching was implemented using the MatchIt package in R, as this approach yielded the greatest overall reduction in standardized mean differences across covariates while retaining all available patients. Covariate balance was assessed using standardized mean differences before and after matching. Progression-free and overall survival were analyzed within the matched sample. Kaplan–Meier survival curves were generated for both progression-free and overall survival and compared between G8 groups using weighted log-rank tests that incorporated the full-matching weights. Cox proportional hazards regression models were fitted to estimate HR and 95% CI for the association between G8 status and survival outcomes. Covariate-adjusted models were estimated, with adjustment for the same variables used in the propensity score model to account for any residual imbalance after matching. The proportional hazards assumption was assessed for the adjusted Cox models using Schoenfeld residuals and formal tests. For the progression-free survival model, several covariates including surgical resection status, FIGO stage, age-adjusted Charlson Comorbidity Index, and age violated the proportional hazards assumption ( $p < 0.05$ ), while G8 status, ECOG performance status, ASA physical status, and BMI did not. Consequently, the progression-free survival model was extended by stratifying on surgical resection status and incorporating time-dependent covariates for FIGO stage, age-adjusted Charlson Comorbidity Index, and age using interaction terms with a function of time. In contrast, for the overall survival model, only surgical resection status violated the proportional hazards

assumption, and the global test was not significant. Therefore, the overall survival model was stratified on surgical resection status without additional time-dependent terms. This approach ensured that the Cox models accounted appropriately for non-proportional hazards, improving the validity of the estimated HR.

The manuscript followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [29].

## 3. Results

257 patients who underwent gynecologic oncology surgery at University Medical Center of the Johannes Gutenberg University Mainz were screened. A total of 77 patients were excluded from the analysis for the following reasons: missing data ( $n = 9$ ), cancelled surgery ( $n = 18$ ), presence of precursor lesions only ( $n = 2$ ), surgical procedures without tumor resection ( $n = 12$ ), diagnostic surgery only ( $n = 9$ ), benign final diagnosis ( $n = 15$ ), other malignancies different from gynecological malignancy ( $n = 8$ ), and withdrawal of consent ( $n = 4$ ). Five included patients were younger than 60 years. Of these, four fulfilled the inclusion criteria based on a BMI  $> 35$  kg/m<sup>2</sup>, while only one patient was included solely on the basis of a clinically frail appearance, with an ECOG performance status of 2 at the time of surgery.

### 3.1. Baseline characteristics and non-cancer mortality risk

Baseline characteristics are summarized in Table 1, comparing the G8 negative and G8 positive cohorts. Patients with a higher ECOG performance status or a higher ASA physical status were more often classified as G8 positive. 59.7% of all G8 positive patients took  $\geq 5$  medication in comparison to only 32.8% in the G8 negative cohort ( $p < 0.001$ ). The G8 positive cohort had more comorbidities and a reduced estimated 10-year survival according to the age-adjusted Charlson Comorbidity Index ( $p = 0.028$ ), as well as a higher non-cancer 5-year mortality risk ( $p < 0.001$ ) according to the Schonberg index, see Table 1.

### 3.2. Survival outcomes

The G8 positive cohort had a reduced progression-free survival ( $p = 0.0012$ ) and overall survival ( $p = 0.0045$ ) after propensity score matching. These survival curves are shown in Fig. 2a. In the propensity score-matched sample, unadjusted weighted Cox models showed that G8 positive patients had significantly higher hazards of progression (progression-free survival: HR = 2.25, 95% CI 1.07–4.74,  $p = 0.033$ ) and death (overall survival: HR = 2.88, 95% CI 1.19–6.99,  $p = 0.019$ ) compared with G8 negative patients. Proportional hazards testing indicated that the proportional hazard assumption was met for both unadjusted models. However, in the adjusted progression-free survival model, several covariates (surgical resection status, FIGO stage, age-adjusted Charlson Comorbidity Index, age) and the global test violated the proportional hazard assumption ( $p < 0.05$ ), whereas the adjusted overall survival model only showed a violation for surgical resection status. These results informed the use of stratified and time-dependent Cox models for adjusted analyses. Because the proportional hazards assumption was violated for several covariates in the adjusted progression-free and overall survival models, stratified and time-dependent Cox models were fitted to address these violations. In these models, G8 positive status remained significantly associated with worse progression-free survival (HR: 1.87, 95% CI: 1.01–3.49,  $p = 0.047$ ). For overall survival, the association with G8 status showed a similar trend but did not reach statistical significance (HR: 2.25, 95% CI: 0.98–5.16,  $p = 0.055$ ). Higher FIGO-stages (HR: 1.64, 95% CI: 1.28–2.09,  $p < 0.001$ ), higher ECOG performance status (HR: 1.69, 95% CI: 1.26–2.26,  $p < 0.001$ ), higher age (HR: 1.04, 95% CI: 1.00–1.07,  $p = 0.04$ ), lower BMI (HR: 0.92, 95% CI: 0.88–0.97,  $p = 0.001$ ) and remaining tumor after surgery (HR: 3.87, CI: 2.20–6.83,  $p < 0.001$ ) independently reduced progression-free survival in multivariable

**Table 1**  
Baseline characteristics.

Parameter	All patients n = 180 (%)	G8 negative n = 118 (%)	G8 positive N = 62 (%)	p-value
<b>Endometrial Cancer</b>	72 (40.0)	53 (44.9)	19 (30.6)	0.398
<b>Ovarian Cancer</b>	71 (39.4)	41 (34.7)	30 (48.4)	
<b>Vulvar Cancer</b>	26 (14.4)	17 (14.4)	9 (15)	0.450
<b>Cervical Cancer</b>	6 (3.3)	4 (3.4)	2 (3.3)	
<b>Vaginal Cancer</b>	5 (2.8)	3 (2.5)	2 (3.3)	0.408
<b>Initial diagnosis</b>	158 (87.8)	102 (86.4)	56 (90.3)	
<b>Loco-regional recurrences</b>	22 (12.2)	16 (13.6)	6 (9.7)	0.510
<b>FIGO stage</b>				
FIGO I	80 (44.4)	54 (45.8)	26 (41.9)	0.190
FIGO II	17 (9.4)	13 (11.0)	4 (6.5)	
FIGO III	62 (34.4)	36 (30.5)	26 (41.9)	0.274
FIGO IV	21 (11.7)	15 (12.7)	6 (9.7)	
<b>Histological grading</b>				0.013
G1	25 (13.9)	18 (15.3)	7 (11.3)	
G2	42 (23.3)	33 (28.0)	9 (14.5)	0.015
G3	33 (18.3)	22 (18.6)	11 (17.7)	
Unknown	80 (44.4)	45 (38.1)	35 (56.5)	0.060
<b>Chronological age [years] Median (IQR)</b>	68 (64–74.5)	68 (63.8–73)	68.5 (64–77.3)	
<b>Chronological age [years] Mean (± SD)</b>	69.6 (± 7.9)	68.9 (± 7.6)	70.8 (± 8.3)	0.028
<b>Body Mass Index [kg/m<sup>2</sup>] Mean (± SD)</b>	28.0 (± 7.1)	28.1 (± 6.0)	27.9 (± 8.8)	
<b>ECOG Performance Status</b>				<0.001
0	80 (44.4)	59 (50.0)	21 (33.9)	
1	66 (36.7)	44 (37.3)	22 (35.5)	0.028
2	19 (10.6)	10 (8.5)	9 (14.5)	
3	13 (7.2)	4 (3.4)	9 (14.5)	0.028
4	1 (0.6)	–	1 (1.6)	
Unknown	1 (0.6)	1 (0.8)	–	<0.001
<b>ASA Physical Status</b>				
0	–	–	–	0.028
1	2 (1.1)	2 (1.7)	–	
2	86 (47.8)	65 (55.1)	21 (33.9)	0.028
3	86 (47.8)	49 (41.5)	37 (59.7)	
4	6 (3.3)	2 (1.7)	4 (6.5)	0.028
4	6 (3.3)	2 (1.7)	4 (6.5)	
<b>Polypharmacy ≥ 5</b>	59 (32.8)	22 (18.6)	37 (59.7)	0.028
<b>Age-adjusted Charlson Comorbidity Index*</b>				
Low risk (0–1 points)	4 (2.2)	3 (2.5)	1 (1.6)	0.028
Intermediate risk (2–3 points)	110 (61.1)	79 (66.9)	31 (50.0)	
High risk (≥4 points)	66 (36.7)	36 (30.5)	30 (48.4)	0.028
<b>Age-adjusted Charlson-Comorbidity Index* estimated 10-year survival</b>				
98%	1 (0.6)	1 (0.8)	–	0.028
96%	3 (1.7)	2 (1.7)	1 (1.6)	
90%	62 (34.4)	45 (38.1)	17 (27.4)	0.028
77%	48 (26.7)	34 (28.8)	14 (22.6)	
53%	34 (18.9)	22 (18.6)	12 (19.4)	0.028
21%	18 (10)	10 (8.5)	8 (12.9)	
2%	11 (6.1)	2 (1.7)	9 (14.5)	0.028
0%	3 (1.7)	2 (1.7)	1 (1.6)	
<b>Risk of 5-year non-cancer mortality according to Schonberg Index (ePrognosis)*</b>				<0.001
<3%	30 (16.7)	27 (22.9)	3 (4.8)	
3–6%	40 (22.2)	30 (25.4)	10 (16.1)	0.028
7–8%	32 (17.8)	24 (20.3)	8 (12.9)	
10–12%	32 (17.8)	21 (17.8)	11 (17.1)	0.028
9–15%	4 (2.2)	2 (1.7)	2 (3.2)	
17–27%	18 (10.0)	10 (8.5)	8 (12.9)	0.028
26–29%	11 (6.1)	1 (0.8)	10 (16.1)	
37–41%	4 (2.2)	2 (1.7)	2 (3.2)	0.028
47–52%	4 (2.2)	–	4 (6.5)	
60–61%	2 (1.1)	–	2 (3.2)	0.028
>70%	2 (1.1)	–	2 (3.2)	
N/A	1 (0.6)	1 (0.8)	–	

ASA: American Society of Anesthesiologists; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; IQR: interquartile range; SD: standard deviation.

\* Age-adjusted Charlson-Comorbidity-Index and Schonberg index were calculated without the current cancer diagnosis to assess the patient's general life expectancy/mortality rate.

Cox-regression analysis. In multivariable Cox-regression analysis, including G8-score, ECOG performance status, ASA physical status, FIGO-stage, BMI, age, age-adjusted Charlson Comorbidity Index (1–3), surgical resection status (R0 vs. R1/2), only ECOG performance status (HR: 2.02, 95% CI: 1.42–2.89,  $p < 0.001$ ), BMI (HR: 0.85, 95% CI: 0.80–0.91,  $p < 0.001$ ) and surgical resection status (HR: 7.29, 95% CI: 3.73–14.27,  $p < 0.001$ ) remained their significant influence on overall survival. The timing of surgery, whether at initial diagnosis or due to recurrence or progression, had no significant impact on overall survival in the univariable Cox regression analysis. All data are listed in Table 3.

### 3.3. Perioperative outcomes

The surgical approach was comparable within both cohorts, see Table 2 for all treatment characteristics. The postoperative complication rate, classified with the Clavien-Dindo classification [30], did not differ between both groups ( $p = 0.247$ ). The G8 positive cohort had more re-operations (14.5% vs. 5.1%,  $p = 0.030$ ) and in general a longer hospital stay (13 days vs. 8 days,  $p = 0.028$ ). The mean follow-up was 25 months. The events of tumor recurrence and/or progression during follow-up were comparable in both groups. However, significantly more G8 positive patients died during the follow-up (41.6% vs. 19.5%,  $p = 0.001$ ).

### 3.4. Laboratory/nutritional parameters

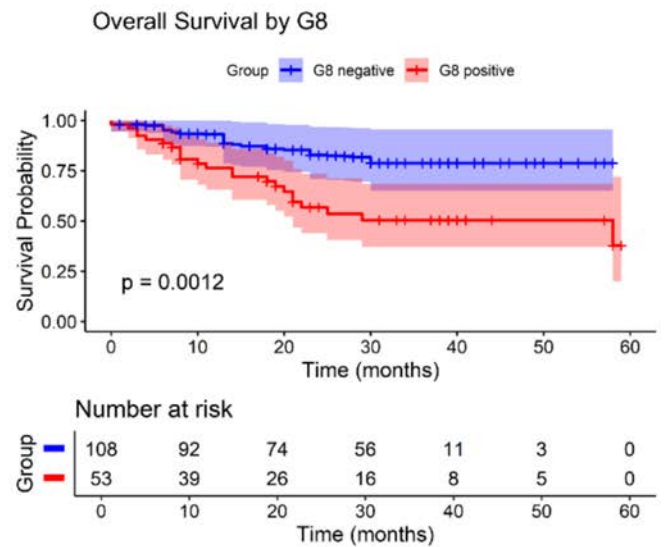
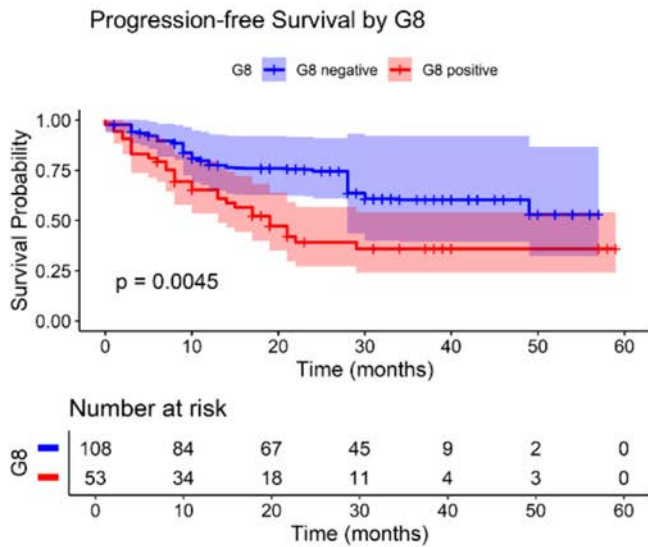
Regarding the laboratory results that were available for 61 patients, 44 patients (72.1%) had vitamin D insufficiency (<30 ng/mL). The G8 positive group had lower vitamin D levels compared to the G8 negative group. Extremely reduced vitamin D levels (<12 ng/mL) appeared to have a negative influence on progression-free survival (75% vs. 92.4%,  $p = 0.051$ ), but this was not statistically significant and had no impact on OS. 5 out of 61 patients had cobalamin deficiency (<200 ng/mL) and more frequent in the G8 positive cohort. 11.7% of all patients had hypoalbuminemia (< 35 g/L), which also occurred more frequently in the G8 cohort (Table 4). Preoperative anemia was present in 22.8% of all gynecologic oncology patients, and 36.6% of all ovarian cancer patients, 13.9% of endometrial cancer patients, in 16.7% of all cervical cancer patients and 12.9% of all vulvar/ vaginal cancer patients before surgery. Preoperative anemia was significantly more frequent among G8 positive patients ( $p < 0.001$ ). 19.7% of all ovarian cancer patients received an intra- or postoperative red blood cell transfusion, followed by 11.1% of all endometrial cancer patients and only 2 of 31 vulvar/ vaginal cancer patients received a red blood cell transfusion. The G8 positive cohort did not receive more red blood cell transfusions than the G8 non-positive cohort. It was irrelevant whether patients had preoperative anemia or received a red blood cell transfusion in terms of progression-free and overall survival after propensity score-matching (Fig. 2b and c).

## 4. Discussion

### 4.1. Summary of main results

Our findings suggest that the clinical value of preoperative G8 screening in gynecologic oncology lies primarily in prognostic stratification rather than in the prediction of short-term perioperative complications. G8 status was associated with survival outcomes and a lower likelihood of receiving guideline-concordant adjuvant therapy. Frailty assessment itself did not directly guide treatment decisions; however, frail patients more frequently declined or were considered unfit for intensive adjuvant therapy, which may partly explain the observed association. Nevertheless, the resection status (R0) was the most important parameter for the oncologic prognosis.

2 a)



2 b)

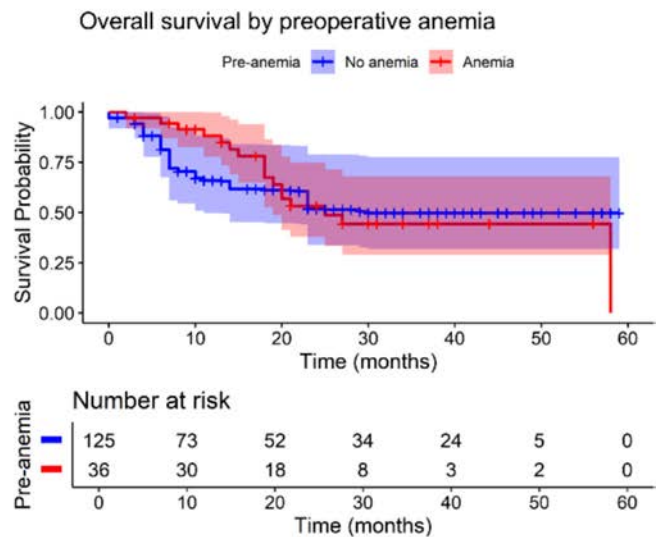
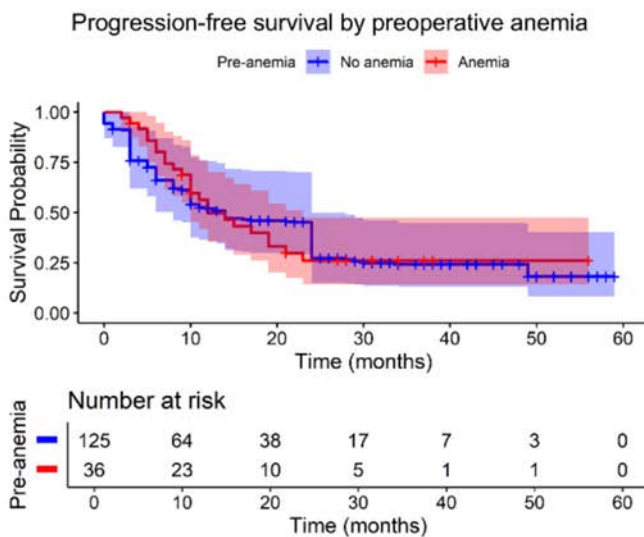


Fig. 2. Propensity score matching.

Preoperative anemia: Hemoglobin <12 g/dL.

RBCt: red blood cell transfusion. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

In contrast to survival outcomes, perioperative complication rates were largely similar between G8 positive and G8 negative patients. This finding suggests that G8 screening may be less suitable for predicting short-term surgical morbidity in this heterogeneous surgical

cohort. A non-significant trend toward a higher rate of severe complications (Clavien-Dindo classification  $\geq 3a$ ) was observed in the G8 positive group. To the best of our knowledge, our study is the first to report an association between lower vitamin D levels and G8 detected frailty.

## 2 c)

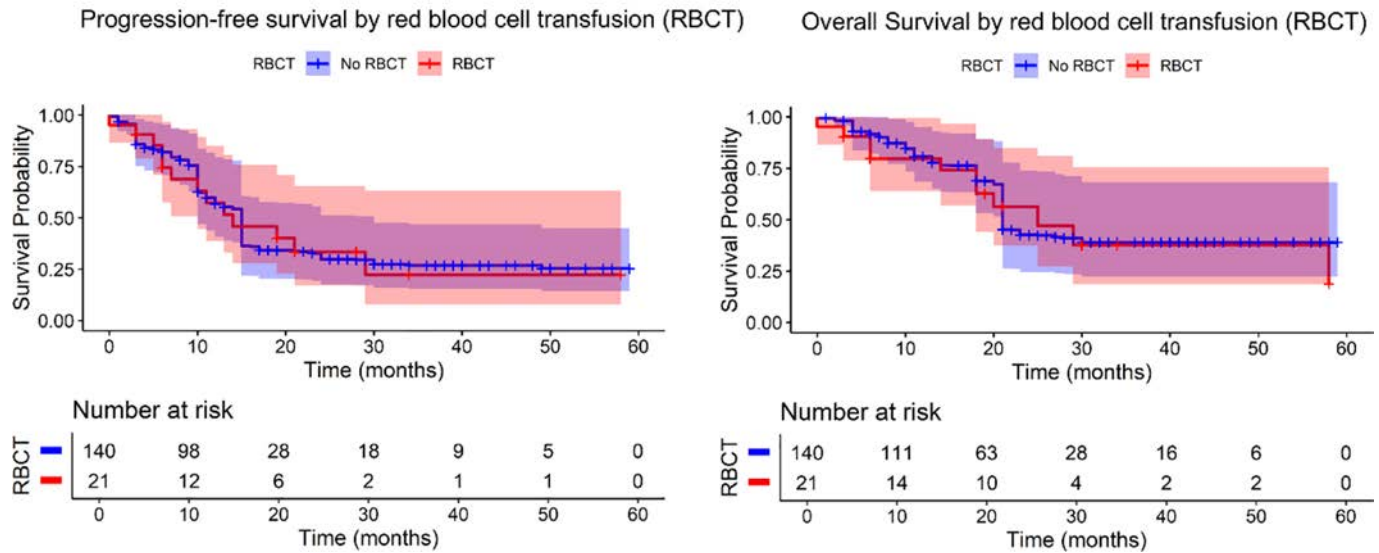


Fig. 2 (continued).

## 4.2. Results in the context of published literature

Our findings support the growing evidence that the G8 screening tool provides prognostic information beyond traditional perioperative risk assessment. Positive G8 scores were associated with reduced overall survival in the ELCAPA (elderly cancer patients) cohort with older cancer patients, regardless of their metastatic status or tumor site [31], thus supporting our results. The current Frail-B study builds on findings from a preceding retrospective analysis, which showed that the G8 score was an independent prognostic factor for both disease-specific survival and overall survival in women over 60 with endometrial cancer. In multivariable analyses, only the G8 score, among several health status tools, retained significant predictive value for survival outcomes [13]. The same retrospective study cohort showed that a positive G8 score was associated with preoperative anemia and perioperative transfusions and more postoperative complications in 153 women  $\geq 60$  years with all stages of endometrial cancer [12]. A high prevalence of preoperative anemia has been observed in patients undergoing gynecologic oncologic surgery and has been linked to an elevated risk of perioperative complications [32]. In our study, preoperative anemia was present in 22% of all gynecologic oncology patients and aligns with the reported 23.1% of preoperative anemia among 60,017 patients undergoing surgery by a gynecologic oncologist. Beyond anemia, which has been associated with reduced overall survival and impaired health-related quality of life in individuals over 60 years of age but not in younger populations [33], other potentially modifiable factors have been implicated in frailty. Vitamin B12 is essential for nerve function and erythropoiesis, although its role in frailty prevention remains unclear [10]. Vitamin D, which is important for bone health and muscle function, has also been linked to frailty risk; however, evidence regarding the benefit of supplementation remains heterogeneous [10]. Regarding vitamin D sufficiency, it was commonly defined as serum 25(OH)D levels  $\geq 30$  ng/mL and with levels between 20 and 29 ng/mL considered insufficient [25]. However, the Endocrine Society has revised its position and no longer endorses fixed thresholds for defining vitamin D insufficiency or sufficiency. Levels below 12 ng/mL are generally accepted as deficient due to associated skeletal risks, while levels  $\geq 20$  ng/mL may be sufficient for bone health. Higher thresholds, including the  $\geq 30$  ng/mL cutoff, lack robust

evidence from randomized trials and are therefore not universally recommended [34,35]. A meta-analysis showed that lower vitamin D levels were significantly associated with increasing frailty severity [11]. In an updated meta-analysis, vitamin D supplementation significantly reduced total cancer mortality but did not reduce total cancer incidence [36]. In addition, the supplementation with vitamin D seemed to reduce the incidence of advanced (metastatic or fatal) cancer in men aged  $\geq 50$  years and women  $\geq 55$  years who were free of cancer and cardiovascular disease at baseline within the VITAL study [37]. On the other hand, a systematic review published in 2024 found no conclusive evidence that vitamin D supplementation improved postoperative outcomes [38]. Overall, frailty prevention in older adults likely requires a multifactorial approach beyond vitamin supplementation alone.

Interestingly, a higher BMI at surgery appeared to be associated with more favorable outcomes in our cohort. While overweight and obesity are generally linked to frailty, several studies have described an obesity paradox, with overweight or low-grade obesity associated with lower mortality in frail or older patients, whereas higher obesity grades may confer increased risk [39–41]. However, evidence in gynecologic oncology remains inconsistent, and these observations warrant further evaluation in prospective studies [40].

## 4.3. Strengths and weaknesses

Key strengths of our study included the use of recent data within the past five years, a prospective design and a follow-up duration exceeding two years. To our knowledge, we report a possible correlation between low G8 scores and low vitamin D levels for the first time. Nevertheless, our study cohort was small and heterogeneous. Patients included both newly diagnosed and recurrent cases from all gynecological entities, which could influence outcomes. Although we applied Cox regression analysis and propensity score matching to strengthen our findings, residual confounding due to limited statistical power was still a problem. Regarding postoperative complications it should be noted that especially small complications for Clavien-Dindo classification grade 1 were difficult to assess. Therefore, Clavien-Dindo classification grade 1 complications might be underestimated. Furthermore, given the probable underreporting

**Table 2**  
Treatment characteristics.

Parameter	All patients n = 180 (%)	G8 negative n = 118 (%)	G8 positive N = 62 (%)	p-value
<b>Surgical treatment</b>				0.185
Radical local excision	27 (15.0)	17 (14.4)	10 (16.1)	
Laparotomy	90 (50.0)	55 (46.6)	35 (56.5)	
Laparoscopy	62 (34.4)	46 (39.0)	16 (25.8)	
Hysteroscopy	1 (0.6)	–	1 (1.6)	
Sentinel node and/or lymph node debulking	101 (56.1)	70 (59.3)	31 (50)	0.149
<b>Mean operating time [minutes] (±SD)</b>	234 (±129.1)	239.2 (±126.4)	225.7 (±134.7)	0.467
<b>Standard-of-care surgical therapy</b>				0.124
Yes	155 (86.1)	105 (89.0)	50 (80.6)	
No	25 (13.9)	13 (11.0)	12 (19.4)	
<b>Standard-of-care adjuvant therapy</b>				<b>0.003</b>
Yes	148 (82.2)	104 (88.1)	44 (71.0)	
No	29 (16.1)	12 (10.2)	17 (27.4)	
<b>Clavien-Dindo classification</b>				0.247
0	68 (37.8)	50 (42.2)	18 (29.0)	
I	33 (18.3)	21 (17.8)	12 (19.4)	
II	38 (21.1)	24 (20.3)	14 (22.6)	
IIIa	18 (10.0)	13 (11.0)	5 (8.1)	
IIIb	16 (8.9)	7 (5.9)	9 (14.5)	
IVa	3 (1.7)	1 (0.8)	2 (3.2)	
IVb	1 (0.6)	–	1 (1.6)	
V	3 (1.7)	2 (1.7)	1 (1.6)	
<b>Re-operation</b>	15 (8.3)	6 (5.1)	9 (14.5)	<b>0.030</b>
<b>Mean length of hospitalization [days] (±SD)</b>	9.9 (±11.9)	8.2 (±6.6)	13.2 (±17.7)	<b>0.028</b>
<b>Readmission rate</b>	13 (7.2)	7 (5.9)	6 (9.7)	0.356
<b>Median follow-up period [months] (IQR)</b>	23 (11–37.8)	26.5 (12–38)	20 (9.5–31.5)	0.092
<b>Mean follow-up period [months] (±SD)</b>	25.1 (±16.3)	26.6 (±16.5)	22.3 (±15.5)	
<b>Recurrence/ tumor progress during follow-up</b>	61 (33.9)	36 (30.5)	25 (40.3)	0.186
<b>Death</b>	49 (27.2)	23 (19.5)	26 (41.6)	<b>0.001</b>
Cancer-related	35 (19.4)	15 (12.7)	20 (32.2)	
Treatment-related	4 (2.2)	3 (2.5)	1 (1.6)	
Other causes	–	–	–	
Unknown	10 (5.6)	5 (4.2)	5 (8.1)	

IQR: interquartile range; SD: standard deviation.

and underestimation of comorbid conditions, prognostic tools such as age-adjusted Charlson Comorbidity Index should be applied and interpreted with caution. Although systematic screening was intended, some eligible patients may not have been screened due to routine clinical constraints or declined participation. Moreover, this study included a heterogeneous range of surgical procedures, encompassing both major and minor gynecologic oncology surgeries, which may have influenced perioperative outcomes and should be

considered when interpreting the results. Gynecologic oncologic surgeons were involved in the establishment of the study and in the perioperative care.

#### 4.4. Implications for practice and future research

Our findings suggest that preoperative G8 screening can serve as a pragmatic first step to identify vulnerable gynecologic oncology

**Table 3**

Cox's proportional hazards model of selected parameters and relationship to progression-free and overall survival.

	Univariable progression-free survival			Multivariable progression-free survival			Univariable overall survival			Multivariable overall survival		
	HR	CI [95%]	p value	HR	CI [95%]	p value	HR	CI [95%]	p value	HR	CI [95%]	p value
Age at surgery	1.05	1.02–1.08	<0.001	1.04	1.00–1.07	<b>0.042</b>	1.07	1.03–1.10	<0.001	1.04	1.00–1.08	0.058
BMI	0.93	0.90–0.97	<0.001	0.92	0.88–0.97	<b>0.001</b>	0.90	0.85–0.95	<0.001	0.85	0.80–0.91	<b>p &lt; 0.001</b>
ECOG Performance Status	1.29	1.04–1.60	<b>0.024</b>	1.69	1.26–2.26	<0.001	1.46	1.12–1.90	<b>0.006</b>	2.02	1.41–2.89	<b>p &lt; 0.001</b>
G8 score (>14 points vs. ≤14)	1.82	1.15–2.86	<b>0.010</b>	1.14	0.67–1.95	0.63	2.44	1.38–4.28	<b>0.002</b>	1.35	0.71–2.58	0.37
Age-adjusted Charlson-Comorbidity Index* (low, intermediate, high risk)	1.33	0.87–2.04	0.19				1.84	1.07–3.17	<b>0.028</b>	1.07	0.47–2.42	0.88
FIGO stages (1–4)	1.68	1.37–2.06	<0.001	1.64	1.28–2.09	<0.001	1.36	1.06–1.73	<b>0.015</b>	1.25	0.91–1.72	<b>0.167</b>
Primary tumor surgery vs. recurrence/progress surgery	2.01	1.12–3.60	<b>0.019</b>	1.13	0.58–2.22	<b>0.72</b>	1.78	0.86–3.67	0.12			
ASA Physical Status (ASA ≤2 vs ASA >2)	1.21	0.83–1.77	0.33				1.60	1.00–2.54	<b>0.050</b>	1.21	0.67–2.21	0.53
Surgical resection status (R0 vs. R1/2)	4.64	2.75–7.83	<0.001	3.87	2.20–6.83	<0.001	4.98	2.68–9.27	<0.001	7.29	3.73–14.27	<b>p &lt; 0.001</b>

ASA: American Society of Anesthesiologists; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; HR: Hazard Ratio; IQR: interquartile range.

\* age-adjusted Charlson-Comorbidity-Index was calculated without the current cancer diagnosis to assess the patient's general life expectancy/ mortality rate.

**Table 4**  
Biochemical and hematological parameters.

Parameter	All patients N (%)	G8 negative N (%)	G8 positive N (%)	p-value
<b>Preoperative Hb-level in mg/dL (<math>\pm</math>SD)</b>	N = 180 13.1 ( $\pm$ 1.6)	N = 118 13.4 ( $\pm$ 1.6)	N = 62 12.4 ( $\pm$ 1.4)	<b>&lt;0.001</b>
<b>Preoperative Anemia &lt;12 g/dL</b>	N = 180 41 (22.8)	N = 118 19 (16.1)	N = 62 22 (35.5)	<b>0.003</b>
<b>Red blood cell transfusion</b>	N = 180 24 (13.3)	N = 118 13 (11.0)	N = 62 11 (17.7)	0.207
<b>Albumin in g/L (<math>\pm</math>SD)</b>	N = 171 39.3 ( $\pm$ 4.2)	N = 110 39.9 ( $\pm$ 4.3)	N = 61 38.1 ( $\pm$ 3.9)	<b>0.001</b>
<b>Albumin &lt;35 g/L</b>	N = 171 21 (11.7)	N = 110 9 (7.6)	N = 61 12 (19.4)	<b>0.028</b>
<b>Vitamin D in ng/mL</b>	N = 61 25.0 ( $\pm$ 19.7)	N = 40 28.5 ( $\pm$ 20.9)	N = 21 18.3 ( $\pm$ 15.5)	<b>0.008</b>
<30 ng/mL	44 (72.1)	27 (67.5)	17 (81.0)	
20–30 ng/mL	16 (26.2)	13 (32.5)	3 (14.3)	
<12 ng/mL	16 (26.2)	6 (15.0)	10 (47.5)	
<b>Vitamin B12 in pg/mL (<math>\pm</math>SD)</b>	N = 61 404 ( $\pm$ 191.5)	N = 40 447 ( $\pm$ 207.9)	N = 21 323.5 ( $\pm$ 123.1)	<b>0.009</b>
<200 pg/mL	5 (8.2)	2 (5.0)	3 (14.3)	

Hb: hemoglobin; SD: standard deviation.

patients who may be at increased risk for poorer oncologic outcomes and treatment de-escalation. Importantly, the G8 should be understood as a prescreening tool that helps identify patients who may benefit from a more comprehensive geriatric assessment. While G8 positivity was associated with poor survival, preoperative anemia, and vitamin D deficiency, the benefit of targeted interventions based on these findings remains uncertain and requires prospective evaluation. Given its simplicity and feasibility, the G8 may facilitate the integration of frailty assessment into routine clinical practice, particularly in resource-limited settings. Future studies should focus on evaluating structured care pathways in which G8 screening is followed by geriatric assessment and targeted interventions.

## 5. Conclusion

A positive G8 screening result preoperatively identified gynecologic oncology patients at increased risk for reduced progression-free and a non-significant trend toward worse overall survival. This study is the first to suggest an association between low vitamin D levels and G8-detected frailty. In addition, preoperative anemia was more frequent among G8 positive patients. These findings highlight the relevance of implementing G8 screening in the preoperative assessment to identify vulnerable patients early, who could benefit from targeted interventions. However, this should be evaluated in prospective studies before clinical benefit can be assumed.

## Statement of ethics

Ethical approval for this study was obtained from the State Medical Association of Rhineland-Palatinate (ID: 16691). The study is registered at German Clinical Trials Register (DRKS00032361). Informed consent was obtained for pseudonymized patient information prior to study inclusion.

## Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author used ChatGPT in order to correct grammatical mistakes for some passages. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the publication.

## Funding sources

This study was not supported by any sponsor or funder.

## Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this work the corresponding author used ChatGPT to check grammar, spelling and to improve the phrasing of certain passages. After using this tool, the author reviewed and edited the content as needed and takes full responsibility for the content of the published article.

## Authors contribution

Conceptualization: VCL, KG, MM. Data acquisition: VCL, EL, LH. Formal analysis: VCL, MSche. Writing-Original Draft: VCL, MSche. Writing-Review and Editing: VCL, EL, LH, KG, MSche., MM, MWS., MSchm, AH. All authors reviewed the manuscript.

## Declaration of competing interest

K. Gillen reports personal fees by Intuitive Surgery, Clovis Oncology, AstraZeneca, Pharma Mar, MSD, GSK, Novartis and Eisai, not related to this trial.

A. Hasenburg reports honoraria and expenses from AstraZeneca, Art Tempi, Celgen, GSK, Lilly, LEO Pharma, MedConcept GmbH, Med update GmbH, Medical Event Solution GmbH, Pfizer, PharmaMar GmbH, Pierre Fabre Pharma GmbH, Roche Pharma AG, Streamedup! GmbH, Tesario as well as work as a consultant to AstraZeneca, GSK, LEO Pharma, Lilly, MSD PharmaMar, Roche, Pfizer, Streamedup! GmbH, Tesario. None were related to this study.

V. Linz reports personal honoraria and expenses from Novartis and Lilly. None were related to this study.

M. Mohr reports personal fees from Pfizer, Novartis and Bristol Myers Squibb. None were related to this study.

Marcus Schmidt reports receiving personal fees from AstraZeneca, BioNTech, Daiichi Sankyo, Eisai, Eurobio, Exact Sciences, Gilead, Lilly, Menarini-Stemline, Molecular Health, MSD, Novartis, Pantarhei Bioscience, Pfizer, Pierre Fabre, and Roche. His institution has received research funding from AstraZeneca, BioNTech, Eisai, Genentech, the German Breast Group, Novartis, Palleos, Pantarhei Bioscience, Pfizer,

Pierre Fabre, and Roche. He is also listed as an inventor on patents EP 2390370 B1 and EP 2951317 B1. None were related to this study.

## Acknowledgments

We sincerely thank Nicole Göllner and Sabine Kaiser for their invaluable support in patient screening and for their dedicated contributions to this study. We are also deeply grateful to all women and their families who participated in the study.

## Data availability

The data supporting the findings of this study are not publicly available, as they contain information that could compromise the privacy of the research participants. Data are available from the corresponding author VCL upon reasonable request.

## References

- M.M. Mullen, T.R. McKinnish, M.A. Fiala, A.S. Zamorano, L.M. Kuroki, K.C. Fuh, et al., A deficit-accumulation frailty index predicts survival outcomes in patients with gynecologic malignancy, *Gynecol. Oncol.* 161 (3) (2021) 700–704.
- E.O. Hoogendijk, J. Afilalo, K.E. Ensrud, P. Kowal, G. Onder, L.P. Fried, Frailty: implications for clinical practice and public health, *Lancet* 394 (10206) (2019) 1365–1375.
- A. Clegg, J. Young, S. Iliffe, M.O. Rikkert, K. Rockwood, Frailty in elderly people, *Lancet* 381 (9868) (2013) 752–762.
- W. Dale, H.D. Klepin, G.R. Williams, S.M.H. Alibhai, C. Bergerot, K. Brintzenhofesoc, et al., Practical assessment and management of vulnerabilities in older patients receiving systemic cancer therapy: ASCO guideline update, *J. Clin. Oncol.* 41 (26) (2023) 4293–4312.
- S. Rostoft, A. O'Donovan, P. Soubeyran, S.M.H. Alibhai, M.E. Hamaker, Geriatric assessment and management in cancer, *J. Clin. Oncol.* 39 (19) (2021) 2058–2067.
- M. Hamaker, C. Lund, M. Te Molder, P. Soubeyran, H. Wildiers, L. van Huis, et al., Geriatric assessment in the management of older patients with cancer – a systematic review (update), *J. Geriatr. Oncol.* 13 (6) (2022) 761–777.
- M.E. Hamaker, J.M. Jonker, S.E. de Rooij, A.G. Vos, C.H. Smorenburg, B.C. van Munster, Frailty screening methods for predicting outcome of a comprehensive geriatric assessment in elderly patients with cancer: a systematic review, *Lancet Oncol.* 13 (10) (2012) e437–e444.
- C.A. Bellera, M. Rainfray, S. Mathoulin-Pelissier, C. Mertens, F. Delva, M. Fonck, et al., Screening older cancer patients: first evaluation of the G-8 geriatric screening tool, *Ann. Oncol.* 23 (8) (2012) 2166–2172.
- K. Horiuchi, T. Kuno, H. Takagi, N.N. Egorova, D. Afezoli, Predictive value of the G8 screening tool for postoperative complications in older adults undergoing cancer surgery: a systematic review and meta-analysis, *J. Geriatr. Oncol.* 15 (3) (2024), 101656.
- B. Pratumvinit, J. De Biasi, Y. Boonyasit, R. Sutiwisesak, P. Chitta, C. Korsirikoon, et al., Roles of folate, vitamin B(12) and vitamin D in older individuals with frailty, *Nutr. Res. Rev.* 39 (2025), e1.
- D. Marcos-Perez, M. Sanchez-Flores, S. Proietti, S. Bonassi, S. Costa, J.P. Teixeira, et al., Low vitamin D levels and frailty status in older adults: a systematic review and meta-analysis, *Nutrients* 12 (8) (2020).
- K. Anic, F. Flohr, M.W. Schmidt, S. Krajnak, R. Schwab, M. Schmidt, et al., Frailty assessment tools predict perioperative outcome in elderly patients with endometrial cancer better than age or BMI alone: a retrospective observational cohort study, *J. Cancer Res. Clin. Oncol.* 149 (4) (2022) 1551–1560.
- K. Anic, C. Althoefer, S. Krajnak, M.W. Schmidt, R. Schwab, V.C. Linz, et al., The preoperative G8 geriatric screening tool independently predicts survival in older patients with endometrial cancer: results of a retrospective single-institution cohort study, *J. Cancer Res. Clin. Oncol.* 149 (2) (2022) 851–863.
- Anesthesiologists ASO, Statement on ASA Physical Status Classification System, <https://www.asahq.org/standards-and-practice-parameters/statement-on-asa-physical-status-classification-system>; 2025. last update: 19.03.2025.
- M.M. Oken, R.H. Creech, D.C. Tormey, J. Horton, T.E. Davis, E.T. McFadden, et al., Toxicity and response criteria of the eastern cooperative oncology group, *Am. J. Clin. Oncol.* 5 (6) (1982) 649–655.
- S.J. Lee, K. Lindquist, M.R. Segal, K.E. Covinsky, Development and validation of a prognostic index for 4-year mortality in older adults, *JAMA* 295 (7) (2006) 801–808.
- M.A. Schonberg, R.B. Davis, E.P. McCarthy, E.R. Marcantonio, Index to predict 5-year mortality of community-dwelling adults aged 65 and older using data from the National Health interview survey, *J. Gen. Intern. Med.* 24 (10) (2009) 1115–1122.
- L.C. Yourman, S.J. Lee, M.A. Schonberg, E.W. Widera, A.K. Smith, Prognostic indices for older adults: a systematic review, *JAMA* 307 (2) (2012) 182–192.
- S.G. Mohile, W. Dale, M.R. Somerfield, A. Hurria, Practical assessment and management of vulnerabilities in older patients receiving chemotherapy: ASCO guideline for geriatric oncology summary, *J. Oncol. Pract.* 14 (7) (2018) 442–446.
- M.A. Schonberg, R.B. Davis, E.P. McCarthy, E.R. Marcantonio, External validation of an index to predict up to 9-year mortality of community-dwelling adults aged 65 and older, *J. Am. Geriatr. Soc.* 59 (8) (2011) 1444–1451.
- M.E. Charlson, P. Pompei, K.L. Ales, C.R. MacKenzie, A new method of classifying prognostic comorbidity in longitudinal studies: development and validation, *J. Chronic Dis.* 40 (5) (1987) 373–383.
- D. Radovanovic, B. Seifert, P. Urban, F.R. Eberli, H. Rickli, O. Bertel, et al., Validity of Charlson comorbidity index in patients hospitalised with acute coronary syndrome. Insights from the nationwide AMIS plus registry 2002–2012, *Heart* 100 (4) (2014) 288–294.
- H. Quan, B. Li, C.M. Couris, K. Fushimi, P. Graham, P. Hider, et al., Updating and validating the Charlson comorbidity index and score for risk adjustment in hospital discharge abstracts using data from 6 countries, *Am. J. Epidemiol.* 173 (6) (2011) 676–682.
- Anaemias WHOSoN, World Health O, Nutritional Anaemias : Report of a WHO Scientific Group [Meeting Held in Geneva from 13 to 17 March 1967], World Health Organization, Geneva, 1968.
- M.F. Hollick, N.C. Binkley, H.A. Bischoff-Ferrari, C.M. Gordon, D.A. Hanley, R.P. Heaney, et al., Evaluation, treatment, and prevention of vitamin D deficiency: an endocrine society clinical practice guideline, *J. Clin. Endocrinol. Metab.* 96 (7) (2011) 1911–1930.
- A. Hunt, D. Harrington, S. Robinson, Vitamin B12 deficiency, *BMJ* 349 (2014), g5226.
- Team RC, R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria, 2023.
- R. Denz, R. Klaassen-Mielke, N. Timmesfeld, A comparison of different methods to adjust survival curves for confounders, *Stat. Med.* 42 (10) (2023) 1461–1479.
- J.P. Vandenbroucke, E. von Elm, D.G. Altman, P.C. Gotszche, C.D. Mulrow, S.J. Pocock, et al., Strengthening the reporting of observational studies in epidemiology (STROBE): explanation and elaboration, *PLoS Med.* 4 (10) (2007), e297.
- P.A. Clavien, J. Barkun, M.L. de Oliveira, J.N. Vauthey, D. Dindo, R.D. Schulick, et al., The Clavien-Dindo classification of surgical complications: five-year experience, *Ann. Surg.* 250 (2) (2009) 187–196.
- C. Martinez-Tapia, E. Paillaud, E. Liuu, C. Tournigand, R. Ibrahim, V. Fossey-Diaz, et al., Prognostic value of the G8 and modified-G8 screening tools for multidimensional health problems in older patients with cancer, *Eur. J. Cancer* 83 (2017) 211–219.
- O.W. Foley, B. Vega, D. Roque, E. Hinchcliff, J. Marcus, E.J. Tanner, et al., Characterization of pre-operative anemia in patients undergoing surgery by a gynecologic oncologist and association with post-operative complications, *Int. J. Gynecol. Cancer* 33 (11) (2023) 1778–1785.
- H. Wouters, M.M. van der Klauw, T. de Witte, R. Stauder, D.W. Swinkels, B.H.R. Wolffenbuttel, et al., Association of anemia with health-related quality of life and survival: a large population-based cohort study, *Haematologica* 104 (3) (2019) 468–476.
- C.R. McCartney, M.E. McDonnell, M.D. Corrigan, R.W. Lash, Vitamin D insufficiency and epistemic humility: an endocrine society guideline communication, *J. Clin. Endocrinol. Metab.* 109 (8) (2024) 1948–1954.
- M.B. Demay, A.G. Pittas, D.D. Bikle, D.L. Diab, M.E. Kiely, M. Lazaretti-Castro, et al., Vitamin D for the prevention of disease: an endocrine society clinical practice guideline, *J. Clin. Endocrinol. Metab.* 109 (8) (2024) 1907–1947.
- N. Keum, D.H. Lee, D.C. Greenwood, J.E. Manson, E. Giovannucci, Vitamin D supplementation and total cancer incidence and mortality: a meta-analysis of randomized controlled trials, *Ann. Oncol.* 30 (5) (2019) 733–743.
- P.D. Chandler, W.Y. Chen, O.N. Ajala, A. Hazra, N. Cook, V. Bubes, et al., Effect of vitamin D3 supplements on development of advanced cancer: a secondary analysis of the VITAL randomized clinical trial, *JAMA Netw. Open* 3 (11) (2020), e2025850.
- A. Patel, E.J. Caruana, J. Hodson, R. Morrison, B. Khor, S. Gysling, et al., Role of vitamin D supplementation in modifying outcomes after surgery: a systematic review of randomised controlled trials, *BMJ Open* 14 (1) (2024), e073431.
- K. Jayanama, O. Theou, J. Godin, A. Mayo, L. Cahill, K. Rockwood, Relationship of body mass index with frailty and all-cause mortality among middle-aged and older adults, *BMC Med.* 20 (1) (2022) 404.
- M. Pavone, M. Goglia, C. Taliento, L. Lecointre, N. Bizzarri, F. Fanfani, et al., Obesity paradox: is a high body mass index positively influencing survival outcomes in gynecological cancers? A systematic review and meta-analysis, *Int. J. Gynecol. Cancer* 34 (8) (2024) 1253–1262.
- C. Canales, M. Anderson, D. Elashoff, T. Grogan, M.M. Russell, V. Duval, et al., Body mass index and postsurgical outcomes in older adults, *JAMA Netw. Open* 8 (8) (2025), e2528875.