FMALE SCORE: COMBINING PRACTICAL RISK SCALES TO IMPROVE PREOPERATIVE PREDICTIVE ACCURACY IN EMERGENCY GENERAL SURGERY: A MULTI-CENTRE PROSPECTIVE COHORT STUDY

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Our increasingly aging population is associated with older people being admitted to surgical wards at a rate surpassing population growth. [1] Although frailty is not exclusive to older adults, its prevalence is positively associated with age. [2] Hewitt et al. observed frailty to independently predict increased length of hospital stay (LOS), 30-day and 90-day mortality for adults aged ≥65 years admitted to emergency general surgery (EGS). [3] Recent evidence has shown that the association between frailty and poor outcomes, is not limited to older adults, but extends to all adult EGS patients. [4] Although risk stratification tools have been derived for EGS patients, none have included a measure for frailty. [5] Previously, Ablett et al. suggested the MALE score to identify older patients at risk of poorer outcomes who may benefit from comprehensive geriatric assessment based on four characteristics obtained at the point of care: Male, Anaemic, Low albumin, and age Eight-five and over. [6] We aimed to investigate whether the accuracy of MALE score could be augmented, through incorporating physical frailty defined by the Clinical Frailty Scale (CFS), and applied to all EGS adults.

This multi-centre prospective cohort study included 2,147 adults from the Older Persons Surgical Collaboration (www.OPSOC.eu) admitted to EGS in United Kingdom during May-July 2015 and June-August 2016. Data collectors were trained in CFS usage. Sex, serum haemoglobin, serum albumin, and age were grouped as per MALE score (male vs female; haemoglobin ≤12.9g/dL vs >12.9g/dL; albumin ≤3.5g/dL vs >3.5g/dL; age <85 years vs ≥85 years). [6] CFS ≥5 was defined as frail. [7] We considered the outcomes: 90-day all-cause mortality (primary outcome), 30-day all-cause mortality, 30-day readmission and LOS (>5 days). We developed a specific *a priori* analysis plan and deemed two-sided p <0.05 as statistically significant. We used SPSS, V25.0 (Armonk, NY, IBM Corp) for all analysis.

946 (44.1%) patients were men. The median age is 55 years (IQR 37-72). Median MALE and CFS scores were 1 (IQR 1-2) and 2 (IQR 1-3) respectively. 1 in 8 patients were

frail. 1 in 4 patients received emergency surgery. Logistic regression was performed with covariates MALE variables and CFS against 90-day mortality as the base model (Model A). Model B adjusted for (1) emergency surgical intervention (yes/no) and (2) polypharmacy (≥5); Model C adjusted for MALE variables as appropriate. Besides low haemoglobin levels and CFS=3, all variables remained significantly associated with 90-day mortality in Model C.

We performed multivariable logistic regressions for frailty (CFS 5-7 vs CSF1-4 as reference) against all four outcomes (Model A, B1, B). By stratifying MALE score (1,2,3,4), we found frailty independently and increasingly predicted 90-day and 30-day mortality for every point increment of MALE score >1. Frailty significantly predicted increased LOS for each MALE score, but was not associated with 30-day readmission after adjustments.

To derive FMALE score, we assigned a number for each CFS score by rounding, to the nearest integer, the regression coefficient (β) from the logistic regression of CFS with 90-day mortality. [8] As patients with CFS 7 were few, and to maintain model simplicity, we collapsed the category to group CSF 6-7. Thus, CFS of 1 scored 0, CFS of 2, 3, 4, and 5 each scored 1, and CFS of 6-7 scored 2. Male, anaemia, low albumin, and age ≥85 years each scored 1 as per MALE scoring. The 7-point score produced can be classified into low (0-1), moderate (2-4), and high (5-6), reflecting increase in severity of underlying health conditions and physiological reserve decompensation. The median FMALE score was 2 (IQR 1-3).

We conducted logistic regressions for each increment of FMALE score (0-1 as reference) against all outcomes (Model A, B1, B). We combined FMALE score 5-6 based on clinical relevance to improve statistical stability. We found FMALE score to significantly and increasingly predict mortality outcomes and increased LOS both before and after adjustments (Model B: 90-day mortality: FMALE = 2 (3.21 (1.33 to 7.75); $p = 0.010$); FMALE = 5-6 (45.81 (17.62 to 119.06); $p < 0.001$); 30-day mortality: FMALE = 3 (6.91 (2.27 to 21.07); $p = 0.001$; FMALE = 5-6 (35.48 (10.35 to 121.62); $p < 0.001$); LOS: FMALE = 2 (1.35 (1.04 to

1.75); $p = 0.001$); FMALE = 5-6 (6.05 (3.34 to 10.97); $p < 0.001$)). FMALE score was also significantly associated with 30-day readmission despite MALE score not predicting the outcome in our analysis (Model B: FMALE = 2 (1.77 (1.33 to 2.35); $p < 0.001$); FMALE = 5-6 (2.01(1.06- 3.81); $p = 0.033$). C-statistics showed superiority of FMALE score to MALE score for all outcomes: 90-day mortality (Area = 0.80; 95%CI (0.76 to 0.84)), 30-day mortality (0.81; (0.76 to 0.86)), 30-day readmission (0.56 (0.53 to 0.59)) and increased LOS (0.68; (0.65 to 0.70)). Prognostic accuracy metrics for 90-day mortality suggested a cut-off score of 2 (FMALE ≥3) where model sensitivity and specificity were 77.2% and 68.3% respectively. Hosmer-Lemeshow test for this model was well fitted to data ($p = 1.00$).

FMALE score is, to our knowledge, the first preoperative EGS risk stratification tool derived for operative and non-operative patients ≥18 years old that incorporates a measure of frailty. Using simple patient attributes and routine physiological markers, it provides speed and ease compared to the Charlston Comorbidity Index or ACS-NSQIP universal surgical risk calculator which require complex calculations or online access that may be impractical in acute settings. [5] FMALE score did not include patient comorbidities, instead, we collected surrogate markers highly related to co-morbid burden and disease severity: frailty, anaemia, low albumin, and polypharmacy. Frailty, a measure of physiologic reserve, also reflects patient capacity to tolerate acute illness and potential surgery. We envisaged FMALE score to streamline emergency care and advise clinical decisions. [1,2] We believe FMALE 0-1 patients will recover with few complications. Patients scoring moderately (2-4) may benefit from frequent senior medical staff and multidisciplinary team input. FMALE 5-6 signifies reduced ability to withstand surgical stress; post-operative escalation of care or conservative managements should be considered for these patients. Although our limited data set found higher FMALE scores to relate with poorer outcomes, confirmation of its prognostic value

with larger cohorts is required in the future. We feel FMALE score has potential to improve perioperative care planning by identifying patients requiring additional clinical attention. [9]

Ethical approval

This study complies with the principles stated in the 1964 Declaration of Helsinki and its subsequent amendments. Data collection was part of a service evaluation and was approved by the clinical audit departments and relevant Caldicott guardians of each institution. Ethical approval was not required.

Conflict of interest statement

None.

Author contribution

PKM, BC, and JH conceived the study. KM is the PI of OPSOC (www.opsoc.eu). PYW conducted the literature search, statistical analysis and drafted the manuscript under the supervision of ADA, BC and PKM. BC was the lead study statistician. All authors contributed to interpretation of the results and the writing of this paper. PKM & JH are guarantors.

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