**ORIGINAL ARTICLE** 

# Implementation of a preoperative pathway for patients undergoing major oncologic gastrointestinal surgery

Giovanni Ferrari\*, Michele Mazzola, Pietro Achilli

Division of Minimally-invasive Surgical Oncology, ASST Grande Ospedale Metropolitano Niguarda, Piazza Ospedale Maggiore, 3 20162 Milan, Italy

#### ABSTRACT

Background: In recent year, a constant increase in life expectancy has occurred in the Western world, leading more elder and frail patients to require major abdominal surgery. These frail patients are more prone to develop postoperative complications and are at higher risk of postoperative mortality. A multimodal, multidisciplinary approach has the potential to improve the perioperative care of these patients. Methods: A cohort of consecutive frail patients undergoing major abdominal surgery for pancreatic and esophago-gastric malignancies between March 2015 and February 2016 was selected and retrospectively evaluated using the modified Frailty Index. Surgical outcomes of this group (experimental group) were compared to a control group of frail patients selected according to main diagnosis, surgical procedures, and surgical team, who underwent major abdominal surgery before the introduction of the multidisciplinary approach (March 2013 to February 2014). Results: Between March 2015 and February 2016, 41 frail patients undergoing major abdominal surgery were identified (experimental group) and compared to similar frail patients receiving similar procedures between March 2013 and February 2014 (control group). The two groups were similar in terms of baseline characteristics (age, gender, American Society of Anesthesiology score, and comorbidities, all P > 0.050), main surgical interventions (P = 0.156), main diagnosis (P= 0.060), and tumor stage (P = 0.420). Modified frailty index and other frailty parameters were similar between the two groups (all P > 0.050). Thirty-days and 3-months mortality rates were lower in the experimental group (0% vs. 14% and 0% vs. 28%, P = 0.010 and P < 0.001 respectively). Similarly, patients in the experimental group showed a lower rate of postoperative overall (41% vs. 74%, P = 0.005) and severe (17% vs. 43%, P = 0.020) complications, while postoperative length of stay, readmission rate and post discharge institutionalization were similar between the two groups (all P > 0.05). Conclusion: The development of a multidisciplinary preoperative pathway for frail patients undergoing major oncologic gastrointestinal surgery for esophago-gastric and pancreatic surgery seems to effectively improve postoperative outcomes, with a significant reduction in the rate of postoperative mortality and complications. Furthermore, the implementation of such a pathway could help the perioperative management of these complex patients and facilitates their territorial take in charge.

Key words: oncologic gastrointestinal surgery, pathway, frail patients

#### \*Corresponding Author:

Giovanni Ferrari, MD, Division of Oncologic and Mini-invasive General Surgery, ASST Grande Ospedale Metropolitano Niguarda, Piazza dell'Ospedale Maggiore, 3 20162 Milan, Italy. E-mail: giovanni.ferrari@ospedaleniguarda.it. https://orcid.org/0000-0002-5405-9046

Received: 15 February 2023; Revised: 12 May 2023; Accepted: 7 June 2023; Published: 13 December 2023

https://doi.org/10.54844/hamp.2023.0036

#### INTRODUCTION

Relevant demographic changes have occurred in Western countries through the last decades leading to an increase in the number of patients aged 65 and older. This phenomenon is called the "aging process".<sup>[1]</sup> As a consequence, there is a growing need of caring for older and more complex patients, especially for those affected by tumors.<sup>[2]</sup> Technical and clinical developments have been introduced in the surgical field allowing to offer better standard of care to these patients.<sup>[3,4]</sup> However,

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 International License, which allows others to copy and redistribute the material in any medium or format non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

optimal treatment often consists of major surgical intervention with high risk of postoperative complications.

Several papers have reported outcomes of oncologic surgery in geriatric patients, especially in the field of breast, colorectal, hepato-biliary and lung cancer.<sup>[5–7]</sup>

Frailty, defined as a state of vulnerability characterized by a decline of physiological reserves across multiple organ systems, has emerged as a vital instrument to gain insight into the management of older patients beyond their chronological age.<sup>[8]</sup> Surgical operation represents a tremendous stressor for oncologic patients, and can be even more severe for frail patients, due to their reduced efficiency of homeostatic mechanisms.<sup>[9]</sup> Frail patients undergoing surgery are more likely to encounter adverse surgical outcomes, such as increased postoperative complications and mortality, length of hospital stay and need for postdischarge institutionalization.<sup>[10,11]</sup> Due to the aging process, the number of frail patients is expected to grow, forcing health care systems to search for preoperative tailored management able to prevent adverse complications and to improve clinical outcomes.<sup>[1]</sup>

The Division of General Oncological and Minimally Invasive Surgery of the ASST Grande Ospedale Metropolitano Niguarda in Milan is mainly focused on the diagnosis and treatment of digestive oncological diseases such as colorectal, esophagus-gastric and pancreatic cancer.

At our division, significant improvements have been introduced in daily practice for the care of frail patients, implementing a dedicated pathway for this cohort of patients, both in preoperative and intraoperative settings.

This dedicated pathway for frail patients, integrated in an outpatient pre-hospitalization setting, may allow better preparation for the intervention and planning postoperative care.

## GOALS

Starting from the results of a pilot study which investigated a dedicated pathway for frail patients published by our division in 2017,<sup>[12]</sup> the present paper aims to describe the implementation of a multidisciplinary management for frail patients undergoing major oncological gastrointestinal surgery. The particular pathway of perioperative care aims to improve patients' conditions prior to the intervention, potentially allowing both faster postoperative recovery and better management of potentially occurring complications, as well as a better return to home. The specific aims of this pathway are the following:

(1) identifying frail patients among those candidates for elective major oncological surgery for gastrointestinal neoplasms;

(2) providing adequate patients pre-rehabilitation, according to their clinical conditions, to the type of surgical intervention and to the social context in which they live;

(3) increasing the percentage of patients receiving adequate treatment of their comorbidities before the surgical procedure;

(4) reducing the risk that an incomplete preoperative evaluation will lead to delays or cancellation of surgical interventions;

(5) preventing the consequences of frailty and malnutrition in patients undergoing surgery, such as postoperative complications, lengthening of hospital stays and increased costs;

(6) identifying potential critical patients in order to plan, where necessary, a network of home-based or rehabbased services.

## **METHODS**

Consecutive patients who received preoperative treatment between March 2015 and February 2016 were selected for this study (experimental group). According to main diagnosis, surgical procedures and surgical team, a comparison group (control group) of patients with the same features as the experimental group, was retrospectively selected in the interval between March 2013 and February 2014. No preoperative treatment, in terms of prehabilitation, had been administered to the control group.

Starting from March 2015, all candidates for elective major gastrointestinal surgery were systematically assessed for frailty. There is no limit to age for the selection. Emergent and urgent operations defined as clinical conditions that mandate surgery within 12 hours or between 12 and 72 hours from admission, respectively were excluded. A modified Frailty Index (mFI) described by Robinson et al.<sup>[13]</sup> was used to assess frailty during preoperative surgical evaluation. This mFI analyzed 7 characteristics (Table 1) and for each domain and a 0 or 1 value was attributed. The sum across different domains provided mFI and patients with a score  $\geq 2$  were considered frail. Among several scores available in the literature, the mFI was chosen because of its easy reproducibility and short time request for execution (about 10 minutes).

#### **Table 1: Frailty characteristics**

Characteristics	Experimental group ( $n = 41$ ), $n$ (%)	Control group ( <i>n</i> = 35), <i>n</i> (%)	Р
Test up and go (≥ 15 s)	26 (63)	26 (74)	0.33
Katz score (≥ 1)	8 (19)	11 (31)	0.29
Mini Cog (≤ 3)	27 (66)	15 (43)	0.06
Charlson index (≥ 3)	27 (66)	29 (83)	0.12
Anemia of chronic disease (Ht < 35%)	24 (58)	19 (54)	0.81
Poor nutrition (albumine $< 3.4$ )	13 (32)	13 (37)	0.63
Geriatric syndrome of falls (≥ 1 falls in the 6 months BEFORE the operation)	4 (10)	8 (23)	0.20
Total score			0.28
2	12 (30)	10 (28)	
3	15 (36)	8 (24)	
4	11 (27)	10 (28)	
5	2 (5)	5 (14)	
6	1 (2)	2 (6)	

Note: Data are expressed as number of patients and percentage; they were compared using the Fischer's exact test. P value < 0.05 was considered statistically significant in each test. Total frailty score is reported as number of patients and percentage and was examined by Mann-Whitney U test.

Among frail patients, those affected by esophageal, gastric and pancreatic head malignancies underwent preoperative management which involved a multidisciplinary team composed of surgeon, anesthesiologist, nurse and nutritionist. This subgroup of patients was selected because of a higher risk of postoperative complications.

The preoperative management consisted of immunonutrition-based oral nutritional support. Additional strategies to improve patients' general physical conditions, muscular status and respiratory function were also used to integrate the preoperative management. These included the promotion of positive modifications to the following habits: interruption of smoking, maintaining of respiratory fitness with incentive deep breathing exercise (3 sessions per day of 10 inspiration/expiration cycles), and moderate intensity walking for 30 minutes three times a week.

Primary endpoints were mortality rates at 30 days and 3 months after surgery. Secondary endpoints were overall and severe postoperative complications, length of hospital stay, rates of post-discharge institutionalization and hospital readmission within 90 days.

Complications were defined according to the Dindo-Clavien classification. Complications of grade major than 2 were considered as severe. All gathered data were recorded on an electronic spreadsheet and analyzed using commercially available software, SPSS® software package version 16.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables were examined by Student's *t*-test or Wald's test where appropriate, while proportions were compared using the Fisher's exact test. The Mann-Whitney *U* test was also used for comparison of nonparametric data. A *P* value of < 0.05 was considered statistically significant in each test.

#### RESULTS

More than 150 frail patients were identified during the study period based on the mFI score. Colorectal, pancreatic and esophago-gastric malignancy were diagnosed in 60%, 26% and 16% patients, respectively. Among 79 consecutive patients scheduled for elective curative major surgery for esophagus, stomach and pancreatic head malignancies, 34 patients were assessed as non-frail and 45 as frail. Out of these 45 patients, 4 were subsequently excluded from the study due to evidence of peritoneal carcinomatosis following exploratory laparoscopy/laparotomy. At last, the remaining 41 patients (experimental group) underwent preoperative management followed by curative intent surgery.

Eighty-five patients with the same diagnosis and submitted to comparable surgical procedures between March 2013 and February 2014 were selected. Of them, 35 patients who were found to be frail on the mFI score were enrolled in a control group. Patient characteristics and frailty features of the two groups were reported in Table 1 and Table 2. The most common oncologic diagnosis for both groups were: gastric adenocarcinoma (23 patients and 14 patients in the experimental group and the control group, respectively) and pancreatic head or distal coledhochus adenocarcinoma (10 patients and 13 patients in the experimental group and the control group, respectively). There were no significant differences between the two groups in terms of mean age (P = 0.081), gender (P > 0.9), American Society of Anesthesiology (ASA) score (P = 0.249), main oncological diagnosis (P = 0.058) and neoadjuvant

#### **Table 2: Patient characteristics**

	Experimental group ( $n = 41$ ), $n$ (%)	Control group ( <i>n</i> = 35), <i>n</i> (%)	Ρ
Gender (M/F)	27 (66)/14 (34)	23 (66)/12 (34)	1.00
Mean age (years)	75 (44–90)	75 (59–91)	0.59
ASA score 1–2 3–4	24 (58) 17 (42)	15 (43) 20 (57)	0.24
Main diagnosis Esophago-gastric cancer	31 (76)	19 (57)	0.06
Pancreatic cancer	10 (24)	16 (43)	
Specific diagnosis			0.135
Adenocarcinoma of pancreas/distal choledochus/Vater's ampulla/duodenum	10 (24)	13 (37)	
Gastric adenoca	23 (56)	14 (40)	
Esophago-gastric junction adenoca	6 (15)	2 (6)	
Esophageal adenocarcinoma/ squamocellular carcinoma	1/1 (2.5/2.5)	1/-(3)	
Other neoplasms	_	5 (14)	
Tumor stage T3–T4	33 (80)	25 (71)	0.42
Main surgical intervention			0.156
Pancreatoduodenectomy/total pancreatectomy Partial gastreetomy Total gastreetomiy Esophagectomy	8 (19)/2 (5) 20 (49) 9 (22) 2 (5)	16 (46)/- 12 (34) 7 (20) -	
Neoadjuvant therapy	11 (27)	5 (14)	0.26

Note: Data are compared using the Fischer's exact test. Continuous variables are reported as mean values and range and were examined by Student's *t*-test. P value < 0.05 was considered statistically significant in each test.

treatment (P = 0.260). The groups were also found to be comparable when considering frailty and mFI score (P = 0.281). All patients underwent surgical interventions performed by the same surgeons and no relevant changes had occured in the surgical techniques during the study period.

Postoperative outcomes were reported in detail in Table 3. Lower 30-days mortality (P = 0.018) and 3-months mortality (P < 0.001) after surgery was found in the experimental group when compared to the control group. No fatal events occurred in the experimental group while 15 patients in the control group died of multiple organ failure caused by septic shock after pancreatic resections and esophago-gastrectomy.

Overall and severe complications were significantly lower in the experimental group with a *P* value for each group of 0.005 and 0.021 respectively, whereas no differences were identified between the two cohorts with respect to mean length of hospital stay (P = 0.08), readmission (P = 0.18) and postdischarge institutionalization (P = 0.41).

#### DISCUSSION

This paper describes the implementation of a preoperative pathway to improve the postoperative

outcomes in candidates who were affected by a condition of frailty for major oncologic gastrointestinal surgery on the basis of clinical, laboratory, anamnestic and social characteristics.

As previously pointed out, age is only one of the elements in determining a complex, dynamic and multifactorial condition such as frailty. Therefore, this pathway also includes young patients with important comorbidities or social issues that put them at an increased risk of complications.

Compared to the population selected in the pilot study, the "frailty pathway" also includes patients affected by colorectal neoplasm. Although colorectal resections are generally considered a type of surgery with relatively low-risk complications, frail patients submitted to colon and rectal interventions can face relevant postoperative problems mainly related to ostomy management and requiring postoperative education and rehabilitation. In addition, the multidisciplinary team (already including surgeon, anesthesiologist, nurse and nutritionist) includes Physical Medicine and Rehabilitation of patients at higher risk of cardio-respiratory complications, related to long-lasting bed stay or poor mobilization.

A simple logistic project and a clear organizational plan are crucial aspects of this pathway. Frailty is assessed Table 3: Postoperative outcomes

Results	Experimental group 1 (n = 41), n (%)	Control group ( <i>n</i> = 35), <i>n</i> (%)	Р
30 days mortality <sup>a</sup>	0	5 (14)	0.01
3 months mortality <sup>a</sup>	0	10 (28)	< 0.001
Overall complications <sup>a</sup>	17 (41)	26 (74)	0.005
Type of complication <sup>b</sup>			
Respiratory	4	1	
Cardiovascular	3	7	
Surgical	15	27	
Severe complications <sup>a</sup>	7 (17)	15 (43)	0.02
Type of complication <sup>b</sup>			
Ab ingestis pneumonia	2	1	
Intestinal occlusion	3	_	
Duodenal leakage	1	2	
Esophageal leakage	1	2	
Pancreatic leakage	1	5	
Biliar leakage	1	_	
Septic shock	-	6	
Acute myocardial infarction	-	1	
Abdominal bleeding	-	2	
Intestinal infarction	-	1	
Length of hospital stay	17 (7–76)	27 (8–146)	0.08
Re-admission in hospital <sup>c</sup>	5 (12)	7/25 (28)	0.18
Postdischarge institutionalization	3 (7)	4/25 (16)	0.41

# <sup>a</sup>Data are expressed as number of patients and were examined by using the Fischer's exact test. <sup>b</sup>Data are expressed as single events (one patient could have more than one complication). <sup>c</sup>Continuous variables are reported as median values and range and were examined by Wald's test. *P* value < 0.05 was considered statistically significant in each test.

during pre-hospitalization visit when patients fulfilled the following characteristics:

- (1) age  $\geq$  70 years;
- (2) age < 70 years, with the presence of one of the following conditions:</li>
- (3) significant weight loss (5% of usual body weight in the last 6 months);
- (4) hospitalized patients;
- (5) recent long hospitalization (hospital stay longer than 30 days) or hospitalization in the Intensive Care Unit;
- (6) abnormal Mini Mental Evaluation Test;<sup>[14]</sup>
- (7) presence of the following comorbidities (three in cases of stable condition; two in cases of condition of instability): arterial hypertension, diabetes mellitus, COPD, heart disease, renal failure, vasculopathy, liver disease.

The selected patients are then screened for frailty with the help of validated scoring systems that characterize frailty as a state of age-related decline affecting the following five main domains, according to Linda Freid's definition: unintentional weight loss (shrinking); loss of strength (weakness); lack of energy reported by the patient (exhaustion); limited physical activity (low activity); slow walking speed (slowness). The so-called SHARE-FI scoring system (Survey of Health Aging and Retirement in Europe Frailty Index)<sup>[15]</sup> is routinely used in our center This score can detect the variables identifying the "frailty syndrome", according to Fried, and, by means of summing them and using a specific algorithm, it provides a quantitative value on frailty. This index is available online: http://www.ncbi.ni h.gov/pmc/articles/PMC2939541/pdf/1471-2318-10-5 7.pdf. This score is then integrated with results from other tests administered to patients "at risk of frailty", in order to obtain a multidimensional framework of each patient, as exhaustive as possible.

Based on any abnormal results at the administered tests (ASA score, P-POSSUM, respiratory function test, nutritional biochemical tests, etc.), patients received rehabilitation pathways to improve the compromised function and to be ready to undergo surgery in the best possible condition. These pathways may differ from each other based on the area of greatest frailty of each patient; some patients may need pulmonary rehabilitation, and others may need blood transfusion or other treatments to reduce anemia, or the introduction of new therapies to optimize cardiac function. In this scenario, the presence of a multidisciplinary team is of utmost importance; it is composed mainly by surgeon, anesthesiologist, nurse, nutritionist and rehabilitation physician but may require the intervention of other specialists (cardiologist, pulmonologist, hematologist, internist, nephrologist) to act effectively on specific

	Standard pathway	Frailty pathway	
Postoperative mortality (%)	6	1.2	
Postoperative complications (%)	31.3	20.5	
Postoperative ICU admission (%)	7	3	
Discharge to rehabilitation division (%)	10.8	5	
Mean length of stay (days)	20	13	
Readmission (%)	12	6	

#### dysfunctional areas.

The pathways provide nutritional support for 5–7 days before surgery, regardless of the baseline nutritional risk. In case of high nutritional risk (involuntary weight loss > 10%-15% in the last 6 months; BMI < 18.5 kg/m<sup>2</sup>; value  $\geq 2$  to the Malnutrition Universal Screening Tool; plasma albumin < 3 g/dl), this support lasts at least 10-14 days before surgery. In the majority of patients, nutritional support is carried out with a mixture containing immunomodulating substrates (Impact Oral type). Hospitalization is provided at the Clinical Nutrition facility for adequate nutritional intake through nasojejunal feeding tube in those patients unable to receive oral feeding. Only in extreme cases, parenteral nutrition will be considered.

The pathway also includes a strategy to improve overall physical condition, muscle tone and respiratory function. Smoking cessation, respiratory training by triflow (3 sessions of 10 inhalations/exhalations per day), walking for at least 30 minutes a day are the main interventions provided by our rehabilitation team.

By implementing this multidisciplinary preoperative pathway, we expect to reach the followings achievements:

- (1) Lower postoperative complications;
- (2) Lower postoperative mortality;
- (3) Shorter length of stay;
- (4) Fewer patients needing post-discharge rehabilitation;
- (5) Lower number of patients requiring intensive care unit admission;
- (6) Lower readmissions.

The results expected to be obtained on projections from the pilot study results are shown in Table 4.

The pathway effectiveness is evaluated using the following parameters collected at time of pre-hospitalization, admission, discharge and 30 days after discharge:

(1) General condition of the patient;

- (2) Loss of autonomy/self-sufficiency;
- (3) Length of stay;
- (4) 90-days Postoperative complications;
- (5) Nutritional status.

Interim results will be quarterly discussed during planned multidisciplinary audits. The duration of this trial will last 1 year. At the end of the trial, the results will be analyzed and compared with those reported in the literature, evaluating the opportunity to adopt it definitively in our practice.

#### CONCLUSION

The implementation of a multidisciplinary pathway for frail patients can the careful diagnostic framework of complex patients and the optimization of their conditions before surgery. It aims, on one hand, to reduce the risk of postoperative complications and their sequelae, and on the other side, to better plan patient management in terms of territorial care needs with early activation of services such as integrated home care assistance or accommodation in rehabilitation divisions.

It is also expected to help different specialists in the treatment of complex oncological neoplasm, often difficult to classify nosologically, which forces patients to a continuous wandering between one specialist and another with considerable discomfort for users and economic damage for the company and the NHS in general.

#### DECLARATIONS

#### Author contributions

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Michele Mazzola and Pietro Achilli. The first draft of the manuscript was written by Michele Mazzola and Pietro Achilli and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

#### **Conflict of interest**

The authors have no conflicts of interest to disclose.

#### Data sharing statement

No additional data is available.

# REFERENCES

- Ambler GK, Brooks DE, Zuhir NA, Ali A, Gohel MS, Hayes PD, Varty K, Boyle JR, Coughlin PA. Effect of frailty on short- and midterm outcomes in vascular surgical patients. Br J Surg. 2015 May;102(6):638-45.
- Balducci L, Aapro M. Epidemiology of Cancer and Aging. In: Balducci L, Extermann M. (eds) Biological Basis of Geriatric Oncology. Cancer Treatment and Research, vol 124. Springer, Boston, MA; 2005. pp 1–15.
- Balducci L, Colloca G, Cesari M, Gambassi G. Assessment and treatment of elderly patients with cancer. Surg Oncol. 2010; 19: 117-123.
- PACE participants, Audisio RA, Pope D, Ramesh HS, Gennari R, van Leeuwen BL, West C, Corsini G, Maffezzini M, Hoekstra HJ, Mobarak D, Bozzetti F, Colledan M, Wildiers H, Stotter A, Capewell A, Marshall E. Shall we operate? Preoperative assessment in elderly cancer patients (PACE) can help. A SIOG surgical task force prospective study. Crit Rev Oncol Hematol. 2008; 65: 156-163.
- Kaur P, Santillan AA, McGuire K, Turaga KK, Shamehdi C, Meade T, Ramos D, Mathias M, Parbhoo J, Davis M, Khakpour N, King J, Balducci L, Cox CE. The surgical treatment of breast cancer in the elderly: a single institution comparative review of 5235 patients with 1028 patients ≥70 years. Breast J. 2012; 18: 428-435.

- Hermans E, van Schaik PM, Prins HA, Ernst MF, Dautzenberg PJ, Bosscha K. Outcome of colonic surgery in elderly patients with colon cancer. J Oncol. 2010; 2010: 865908.
- Petrowsky H, Clavien PA. Should we deny surgery for malignant hepato-pancreatico-biliary tumors to elderly patients? World J Surg. 2005; 29: 1093-1100.
- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013; 381: 752-762.
- Ethun CG, Bilen MA, Jani AB, Maithel SK, Ogan K, Master VA. Frailty and cancer: Implications for oncology surgery, medical oncology, and radiation oncology. CA Cancer J Clin. 2017 Sep;67(5):362-377.
- Dasgupta M, Rolfson DB, Stolee P, Borrie MJ, Speechley M. Frailty is associated with postoperative complications in older adults with medical problems. Arch Gerontol Geriatr. 2009; 48: 78-83.
- Lee DH, Buth KJ, Martin BJ, Yip AM, Hirsch GM. Frail patients are at increased risk for mortality and prolonged institutional care after cardiac surgery. Circulation. 2010; 121: 973-978.
- Mazzola M, Bertoglio C, Boniardi M, Magistro C, De Martini P, Carnevali P, Morini L, Ferrari G. Frailty in major oncologic surgery of upper gastrointestinal tract: How to improve postoperative outcomes. Eur J Surg Oncol. 2017; 43: 1566-1571.
- Robinson TN, Wu DS, Pointer L, Dunn CL, Cleveland JC Jr, Moss M. Simple frailty score predicts postoperative complications across surgical specialties. Am J Surg. 2013; 206: 544-550.
- 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 Nov;12(3):189-98.
- Romero-Ortuno R, Walsh CD, Lawlor BA, Kenny RA. A frailty instrument for primary care: findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). BMC Geriatr. 2010; 10: 57.