THE ASSOCIATION BETWEEN FRAILTY, DISCHARGE TO INSTITUTION, AND MORTALITY IN OLDER ADULTS UNDERGOING NON-ELECTIVE ABDOMINAL SURGERY

by

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Submitted in partial fulfilment of the requirements
for the degree of Master of Science

at

Dalhousie University
Halifax, Nova Scotia
June 2013

DALHOUSIE UNIVERSITY

DEPARTMENT OF COMMUNITY HEALTH AND EPIDEMIOLOGY

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Dated: June 25, 2013

Supervisor: _________________________________

Readers: _________________________________

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DALHOUSIE UNIVERSITY

DATE: June 25, 2013

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TITLE:

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DEPARTMENT OR SCHOOL: Department of Community Health and Epidemiology

DEGREE: MSc CONVOCATION: October YEAR: 2013

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Signature of Author

DEDICATION PAGE

For my parents who’ve always supported me even when I was wrong…

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ABSTRACT

The Canadian population is aging and issues related to the care of older adults are becoming increasingly common. The practice of general surgery is no stranger to this phenomenon, as older adults are increasingly presenting for surgery. Some 40% of these surgeries occur on a non-elective basis, which is associated with increased morbidity and mortality when compared to elective surgery. However, very little research has been done on prognostic factors for poor post-operative outcomes in older adults presenting for non-elective surgery. Thus, the purpose of this research is three-fold. First, to review the literature on prognostic factors for adverse outcomes in this patient population. Second, to examine prognostic factors associated with mortality in this patient population. Lastly, to examine prognostic factors associated with discharge to institution in this patient population.

LIST OF ABBREVIATIONS USED

ADL	Activity of Daily Living
ASA	American Society of Anesthesiologists
APACHE-II	Acute Physiology and Chronic Health Evaluation-II
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CDHA	Capital Health District Authority
CGA	Comprehensive Geriatrics Assessment
CHF	Congestive Heart Failure
COPD	Chronic Obstructive Pulmonary Disease
CRF	Chronic Renal Failure
CSHA	Canadian Study of Health and Aging
DM	Diabetes Mellitus
ECOG	Eastern Cooperative Oncology Group
ER	Emergency Room
FI	Frailty Index
GI	Gastrointestinal
HR	Hazard Ratio
IADL	Instrumental Activity of Daily Living
ICU	Intensive Care Unit
IHD	Ischemic Heart Disease
JB	Jonathon Bailey
JS	Jeremy Springer
LOS	Length of Stay
NR	Not reported
NS	Not significant
OR	Odds Ratio
PD	Philip Davis
POSSUM	Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity
QUIPS	Quality in Prognostic Studies
ROB	Risk of Bias
SE	Standard error

ACKNOWLEDGEMENTS

This work would not be possible without the help of several individuals. First and foremost I need to acknowledge Dr. Jonathon Bailey (JB) my partner in crime for two years as we became pseudo-geriatricians, drank, swore, and prayed to God we would never become old. Thank you also to Mr. Jeremy Springer (JS) for your help with the systematic review as well as your youthful enthusiasm. Last, but not least, thank you to my supervisory committee Michele (the optimist), Paul (the pragmatist), and Jill (the realist), for holding the reigns but still giving me enough rope to hang myself.

CHAPTER 1 INTRODUCTION

As the Canadian population ages issues related to the care of older adults (people aged 65 or older) will come to the forefront of health care debate. Currently 14% of the population is aged 65 or older (Figure 1.1), and it is estimated that by the year 2050 this proportion will increase to over 25% (1). This aging population has and will continue to change the way in which health care is delivered, and now more than ever questions about the effectiveness of the health care system need to be asked (2). The practice of general surgery is no stranger to these trends (3). In years past, older adults may have been denied surgery on the basis of age alone, but this is no longer the standard of care (4). Further, recent evidence has shown that older adults undergo abdominal surgery at disproportionate rates, and suffer disproportionate morbidity and mortality, when compared to younger cohorts (5,6). Perhaps, most alarming of all is that the demand for surgery in this population is expected to exceed the rate of this cohort's growth (7).

With increasing age the likelihood of undergoing non-elective (urgent or emergent) abdominal surgery also increases (8,9). Non-elective surgery accounts for over 40% of surgery in this cohort (6), and is associated with a 10-15 fold increase in morbidity (30% vs. 3%) and a 3-5 fold increase in mortality (20% vs. 5%) when compared to elective surgery (4,10-12). Furthermore, non-elective surgery in this cohort is also associated with increased morbidity (28% vs. 10%) and mortality (15.2% vs. 2.5%) when compared to younger cohorts (13,14).

This high potential for poor clinical outcomes can make treatment decisions very difficult (15). While basic outcomes such as living or dying are clearly important, other outcomes such as prolonged hospitalization and institutionalization must be considered.

Research has suggested that the majority of older adults consider quality of life to be as important as its quantity (16,17). End of life decisions are highly influenced by the patients' perceived future health status and perceived chance of the success of interventions (17), providing accurate information about treatment outcomes is an important component of patient counseling. This is especially true in non-elective situations where both information, and time, are limited. As such, surgeons and their patients must presently accept a significant degree of uncertainty when making health care decisions (15). Although, multiple risk assessment tools have been developed over the years (18); their uptake in the clinical setting remains poor. The main reason for this is that currently available risk assessment tools are not sufficiently accurate to predict post-operative outcomes or too time consuming to use (18).

Given the inadequacy of current risk prediction models, it would seem reasonable to consider prognostic factors for negative outcomes in this patient population. Prognostic factors can help to inform care, and can potentially be used to improve quality of care as they facilitate the comparison of health outcomes across institutions and geographic regions through risk adjustment (19). Lastly, prognostic factors can be used in the development of risk assessment models (19). Unfortunately, prognostic factors for outcomes among older adults undergoing non-elective GI surgery remain poorly understood. Furthermore, most studies have focused on morbidity and mortality as opposed to patient centered outcomes including loss of independence and quality of life. Age alone is a poor prognostic factor for health outcomes in this patient population (6,20), and although various prognostic factors (ASA Score, Sex, comorbidities, complications) have been considered there is often inconsistency in reporting and study design. Therefore, in order to understand these relationships more clearly we undertook a systematic review of the literature for prognostic factors for poor outcomes in older adults undergoing non-elective GI surgery (see Manuscript #1).

Recently frailty has emerged as a novel prognostic factor for post-operative outcomes in older adults. Frailty has been defined in many ways, but the most accepted definition sees it as a state of vulnerability arising with age and undermining the ability of an organism to respond to stress (21). Frailty has been shown to be associated with mortality, in older adults undergoing elective abdominal surgery (22); however this relationship remains to be explored in the non-elective setting. Therefore, the purpose of the second paper was to explore the relationship between frailty and mortality in older adults patients undergoing non-elective GI surgery (see Manuscript #2).

During the systematic review process (see Manuscript #1) we noted that no studies explored prognostic factors for discharge to institution in this patient population. Frailty, has been shown to be associated with this outcome in the elective setting (23), but this relationship remains to be explored in the non-elective setting. The purpose of the third paper was to explore the relationship between prognostic factors (including frailty) and discharge to institution (see Manuscript #3).

Thus, the purpose of the research was to: 1. Review the literature on prognostic factors for adverse outcomes in patients undergoing non-elective abdominal surgery, and 2. Examine the relationship between perioperative factors, including frailty, and outcomes after non-elective GI surgery in patients ≥70 years of age.

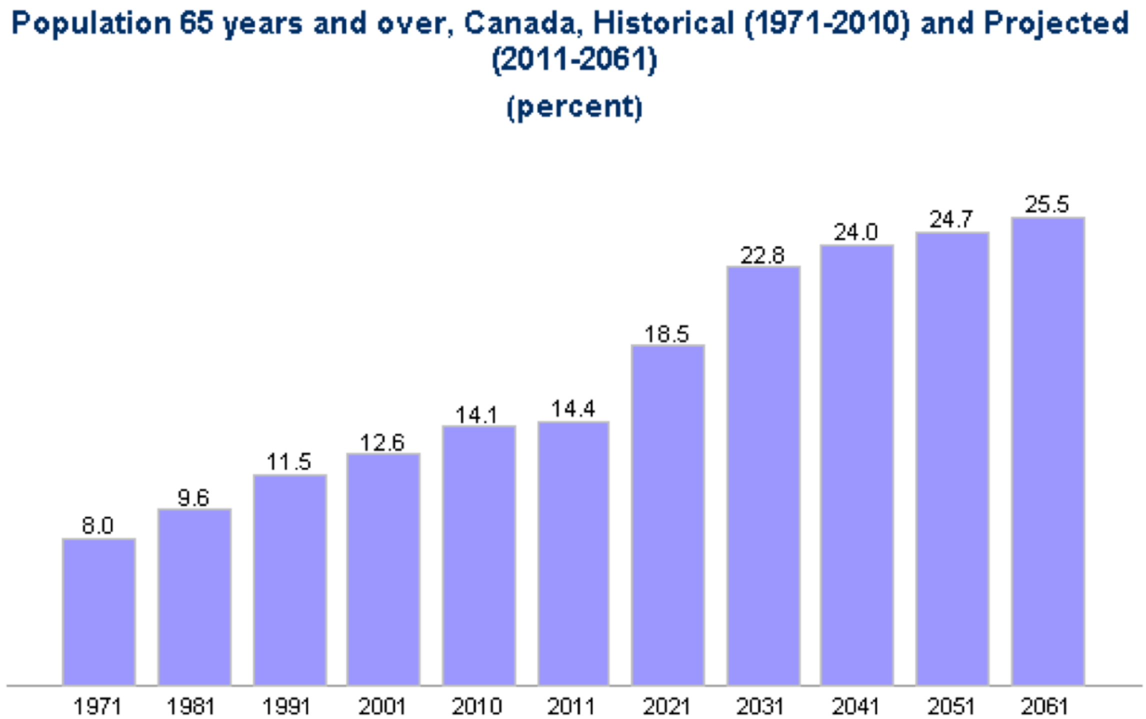

Figure 1.1 Canada's Aging Population

CHAPTER 2 PROGNOSTIC FACTORS FOR MORBIDITY AND MORTALITY IN OLDER ADULTS UNDERGOING NON-ELECTIVE GASTROINTESINAL SURGERY: A SYSTEMATIC REVIEW (MANUSCRIPT ONE)

ABSTRACT

BACKGROUND: Older adults undergoing non-elective GI surgery experience increased morbidity and mortality when compared to younger and elective cohorts. Prognostic factors can be used to counsel patients of these risks and, if modifiable, to minimize them. The purpose of this study was to summarize the literature on prognostic factors for adverse outcomes in elderly patients undergoing non-elective GI surgery.

STUDY DESIGN: PubMed and EMBASE were searched using a strategy developed in collaboration with an expert librarian. Studies that examined independent associations between prognostic factors and morbidity or mortality in patients aged ≥ 65 undergoing non-elective GI surgery were selected. Data were extracted using a standardized form, and quality of studies was assessed using the QUIPS tool.

RESULTS: Nine cohort studies representing 2958 patients satisfied selection criteria. All studies focused on post-operative mortality. A total of 34 prognostic factors were examined and significant variability across studies was noted. Limited or conflicting evidence was found for the majority of prognostic factors examined. Meta-analysis was only possible for the ASA score, which was found to be associated with mortality in four studies (pooled OR = 2.77; 95% CI: 0.92-8.41).

CONCLUSIONS: While non-elective GI surgery in older adults is becoming increasingly common, the literature on prognostic factors for morbidity and mortality in this patient population lags behind. Further research in this area is needed to help guide patient care and potentially improve outcomes.

INTRODUCTION

Older adults (aged ≥ 65) are the fastest growing subset of the population in industrialized countries (24,25). By the year 2040 the proportion of North Americans over the age of 65 is expected to increase to 25% (1). This will impact the delivery of health care, including surgical care, in many ways (3). Of particular concern to the field of general surgery is that 40% of GI surgery in older adults occurs on a non-elective (urgent or emergent) basis (6). Non-elective GI surgery in older adults is associated with increased morbidity and mortality when compared to younger (5,6), and elective cohorts (4,26). This trend has far reaching implications not only for patient care and autonomy, but also for cost and resource planning.

Prognostic factors for perioperative morbidity and mortality are useful to the clinician and patient in several ways (19). At the most basic level prognostic factors can inform care and convey the probability of expected risks to the patient and their family. Second, once identified, factors associated with adverse outcomes can potentially be modified. Lastly, prognostic factors can be used to inform the development of risk prediction models in order to more accurately assess risk for the individual patient. To our knowledge, no previous review articles have explored prognostic factors for this patient population. With these views in mind, the purpose of this study was to systematically review and synthesize the available evidence on prognostic factors associated morbidity and mortality in elderly patients undergoing non-elective GI surgery.

METHODS

Literature Search

A search strategy, developed in collaboration with an expert librarian (see Appendices 1 and 2), was used to search PubMed and EMBASE (all years through June 11, 2012). Search terms (MESH and Emtree headings, as well as free text words), related to non-elective GI surgery, older adults, post-operative outcomes, risk prediction and prognosis were used with Boolean logic to identify all potentially relevant articles. No language restrictions were applied.

Search results were combined using Ref Works™ software (version 2.0, ProQuest), and duplicates were removed. One author (JS) initially screened titles for potential relevance, and citations were excluded if they did not pertain to the study population of interest. Abstracts were independently screened for relevance by two of three reviewers (PD, JS, and JB). Full text review was then performed by two reviewers (JS and PD). At this stage articles were limited to those published in English or French. When there was disagreement about study selection, an attempt at consensus was made. In the rare instance that consensus could not be made adjudication was done by the third reviewer (JB). Reference lists of all included studies were searched for additional studies of potential relevance. If relevant information was unclear or missing up to three attempts were made to contact the primary author to obtain the pertinent information.

Study Selection

Study Population:

Patients aged ≥ 65 undergoing non-elective GI surgery constituted the population of interest. In order to be consistent with current North American models of acute care surgery, included cohorts had to contain at least 90% GI surgery of which at least 75% was non-elective. The definition of non-elective surgery was any "unscheduled" or "unplanned" surgery.

Outcomes of interest:

The primary outcomes of interest were post-operative morbidity and mortality. Post-operative mortality was defined as in-hospital or 30-day mortality. Morbidity was defined as any deviation from the normal post-operative course. Similar to the classification scheme proposed by Dindo et al. 2004, major complications were defined as those requiring surgical, endoscopic or radiologic intervention, and/or complications requiring intensive care (27). Minor complications were defined as any complication, which was not major, including: ileus, wound infection, the need for blood transfusion, systemic infection not requiring intensive care unit (ICU) intervention, cardiac arrthymia or the need for parenteral nutrition. Secondary outcomes of interest were length of stay (LOS), and discharge to an institution (defined as discharge to rehabilitation hospital, assisted living situation or nursing home).

Prognostic Factors:

All prognostic factors evaluated in previous studies were considered in this systematic review. Prognostic factors were classified into three groups for synthesis and clear presentation: 1. Patient factors, 2. Disease factors, and 3. Peri-operative factors. Patient factors were defined as any underlying condition or demographic characteristic present before the acute illness such as age, sex, and comorbidities. Disease factors were any prognostic feature related to the acute illness, such as laboratory values, the presence of sepsis, peritonitis, obstruction, or malignancy. Peri-operative factors were defined as aspects related to the surgical admission such as post-operative complications, time to surgery, need for blood transfusion, and type of surgery.

Study Designs:

Clinical cohort studies were included if there was a longitudinal component between prognostic factor measurement and outcomes of interest, including cohort studies or randomized controlled trials (if analyzed to identify important prognostic variables). Study data could be collected prospectively or retrospectively. Selection of studies was limited to those that included multivariate analysis (studies that reported only univariate, or crude analysis were excluded).

Critical appraisal of included studies

Prognostic factor studies were categorized into three groups based on the phase of investigation (28,29). Phase one studies: exploratory studies in which associations between prognostic factors and outcomes were sought out. Phase two studies: exploratory studies based on prior hypotheses to test the association between prognostic factors and outcomes of interest. Lastly, phase three studies that aimed to explain how relationships between prognostic factors influence the outcome.

ROB was assessed by two reviewers (JB and PD) using the QUIPS tool (30). The QUIPS tool examines ROB in six domains: 1. Study participation, 2. Study Attrition, 3. Prognostic Factor Measurement, 4. Outcome Measurement, 5. Study Confounding and 6. Statistical Analysis and Presentation. Cohen's kappa was used to assess inter-observer reliability for agreement on all six domains. Where there was disagreement about assessment of individual items and judgment about domain risk of bias, reviewers discussed to attempt to reach consensus. In the rare instance that consensus was not made, adjudication was done by a third reviewer (JS).

Data Extraction

Data extraction was performed with consensus by two independent reviewers (PD and JS), using a standardized data extraction form (see Appendix 3). Extracted information included: study characteristics (type of study, number of patients, type of surgery, outcomes of interest), patient characteristics (age, sex, body mass index, and comorbid conditions), and strength of association (odds ratios, relative risks and hazard ratios) between prognostic factors and outcomes of interest.

Data Synthesis

When data were available, multivariate associations between prognostic factors and post-operative outcomes were extracted. For clarity, associations were re-calculated to be in the same direction, as necessary, with associations above 1 indicating a worse prognosis. Where three or more studies reported an association between a prognostic factor and outcome of interest, random-effects generic inverse variance meta-analysis was performed using Review Manager software (RevMan; version 5.1, the Cochrane Collaboration). Standard errors (SE) were calculated from confidence intervals; we appropriately transformed the individual study association and SE to their natural logarithms to normalize their distributions. Heterogeneity between studies was assessed by using X^2 test and I^2. Heterogeneity was considered significant when the X^2 test had a $p<0.10$, or if I^2 was greater than 50%.

Qualitative synthesis of studies was used to explore heterogeneity due to population source and setting, definitions of prognostic factor, and outcomes, where meta-analysis was not possible. Strength of association was defined based on effect size as weak (OR<1.5), moderate (1.5 ≤ OR < 3), or strong (OR ≥ 3). Consistency of findings was assessed using the following schema:

1. **Strong evidence:** Consistent findings (defined as > 75% of studies showing the same direction of effect) in multiple high quality (defined as low ROB in all domains) studies
2. **Moderate evidence:** Consistent findings in multiple low (moderate to high ROB in 4 of 6 domains) quality studies and/or one high quality study
3. **Limited evidence:** One study
4. **Conflicting evidence:** Inconsistent findings across studies
5. **No evidence:** Lack of association between the prognostic factor and outcome of interest.

RESULTS

Nine studies met all of the selection criteria (see Figure 2.1). Sixteen papers (8 Russian, 3 Japanese, 2 German, 1 Chinese, 1 Bulgarian, 1 Norwegian) were excluded as per protocol. The majority of these were published in the late 1970's and early 1980's and did not contain a multivariate analysis. Two additional studies (31,32) were identified through bibliographic review of included studies. Neither was included in the review, as they did not include a multivariate analysis.

Study Characteristics:

Table 2.1 shows the study characteristics of the nine included studies representing a total of 2958 patients (10,20,33-39). Four studies focused exclusively on non-elective colorectal surgery (34-37), while five studies focused on non-elective GI surgery (10,20,33,38,39). All of these studies included mortality as the primary outcome of interest. Two studies examined prognostic factors for morbidity using multivariate analysis (34,36). No included study examined the relationship between prognostic factors, LOS or discharge to institution.

Study Designs:

Table 2.2 summarizes the risk of bias assessment for all included studies. Inter-rater reliability of all six domains was good (k = 0.76; 95% CI: 0.59-0.92). Two studies were prospective cohorts (10,35) and the remainder were retrospective. All studies were exploratory, phase one, investigations. The majority of studies were rated as low to moderate quality. The main issues with potential risk of bias were related to the domains: prognostic factor measurement, study confounding, and statistical analysis. Risk of bias was reported as moderate in seven studies (10,20,33-37) due to incomplete reporting on how prognostic factors were measured. Five studies (10,20,33,36,37) were rated as having moderate risk of bias due to confounding (there was partial reporting on confounder measurement). One study (34) was rated at high risk of bias due to partial reporting on which potential confounders were included in multivariate analyses. Lastly, with respect to statistical analysis, the majority of studies were considered to be at moderate risk of bias as step-wise regression was used. One study was rated at high risk of bias as in addition to using step-wise regression, model presentation, was incomplete (36).

Prognostic factors associated with peri-operative mortality:

Patient factors associated with post-operative mortality in the included studies are summarized in Table 2.3. A total of nine patient factors were investigated across studies. There is limited evidence of an association between a history of COPD (35), a history of CHF (35), dependent functional status (35) and mortality. All studies examined age as a prognostic factor. Evidence for an association between age and mortality was conflicting as only four studies (10,35-37) found an association on multivariate analysis (5 studies reported negative/neutral associations with outcome). The ASA score was considered in seven of nine studies (10,20,34,36-39) and results were also inconsistent. Three studies treated the ASA score as an ordinal variable and a pooled analysis is summarized in Figure 2.2 (pooled OR=2.77; 95% CI: 0.92-8.41). Contradictory evidence also existed for sex sex (10), and a history of neurological disease (37). There is no evidence of an association between the ECOG physical status and mortality.

Disease factors associated with post-operative mortality are summarized in Table 2.4. A total of eleven disease factors were analyzed. There was limited evidence of an association between the Physiological Score (PS) of the POSSUM (Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity) score (33), the neutrophil to lymphocyte (N/L) ratio (39), ≥ 2 failing organs (38) and mortality. Conflicting evidence for an association between mortality and serum creatinine (35,36), mesenteric ischemia (20,35,37), the presence of SIRS or sepsis (10,35-37), and metastatic disease (20,35,37,38) was shown. There was no evidence of an association between the APACHE-II score (33), the Operative Severity Score (OSS) of the POSSUM score (33), the presence of GI bleeding (20,35,37), intestinal obstruction (10,20,35), or the presence of peritonitis (20,37) and mortality.

Peri-operative factors associated with patient mortality are summarized in Table 2.5. A total of fourteen peri-operative factors were considered across studies. There was moderate evidence of an association between duration of symptoms prior to admission and mortality (20,33). There was limited evidence for an association between mortality and palliative resection (20), non-therapeutic laparotomy (20), need for invasive monitoring (10), need for ICU (10), and midline laparotomy (39). Conflicting evidence for an association between time from admission to surgery(20,36-38), post-operative complications (34,36-38), pre-operative steroid use (35,36), estimated blood loss (36,37) was shown. There was no evidence of an association between GI resection (10,20,34,35), suture repair of perforation (20,34), time from symptom onset to OR (20), or adequate resuscitation (10) and mortality.

Prognostic factors associated with post-operative complications:

Only two exploratory studies examined potential prognostic factors for post-operative morbidity (19,21). One study (34) evaluated the association between patient age, sex, surgeons' expertise, ASA grade, hemoglobin on admission, the need for blood transfusion, duration of the operation, and type of operation and post-operative morbidity. On multivariate analysis only high ASA score (≥3) was associated (OR = 37.29; 2.31-602.60) with postoperative morbidity. A second study (36) examined the relationship between seventeen prognostic factors and the development of any post-operative complication (including pneumonia, respiratory failure, myocardial infarction, deep venous thrombosis, pulmonary embolus, and stroke). They used a step-wise regression model and found wound contamination (OR=3.22; 1.55-6.67 p<0.001), shock (OR = 2.23; 1.05-4.88, p=0.04), chronic renal insufficiency (OR = 1.47; 1.06-2.04, p=0.02) and time in operating room (no OR reported as data continuous, p=0.01) to be associated with post-operative complications.

Taken together, these studies provide limited evidence of an association between an ASA score ≥3, wound contamination, shock, chronic renal insufficiency, time in operating room and post-operative morbidity in this patient population.

DISSCUSSION

As the population ages, issues related to the surgical care of the elderly are becoming increasingly common (4,6,14,25). Accordingly, there has been considerable interest in risk assessment for elderly patients undergoing abdominal surgery (18,40-42). However, currently available pre-operative risk assessment tools including the ASA score (43), APACHE-II score (44), as well as several other models (45-52) lack sufficient accuracy and reliability and often are not applicable in the non-elective clinical setting in this patient population (18,39,40). Better risk prediction models are needed to guide the care of older patients, particularly in areas associated with high morbidity and mortality (53).

To our knowledge, this is the first systematic review on prognostic factors associated with mortality among older adults undergoing non-elective GI surgery. A total of 34 potential prognostic factors were analyzed and there was significant variability with regards to which factors were examined in each study. The majority of evidence suggesting an association between prognostic factors and mortality was limited or conflicting. Only age at surgery, the ASA score, the presence of SIRS/Sepsis, duration of symptoms prior to admission, and post-operative complications were shown to be associated with mortality in more than one study. Quantitative meta-analysis was only possible for the ASA score (10,20,37). There was significant heterogeneity in effect size (I^2=92%) and the results are heavily weighted in favor of one study (20).

Although there was an association between increased ASA score and post-operative mortality in older adults undergoing acute abdominal surgery, four studies not incorporated in the quantitative meta-analysis did not show an association between ASA score and mortality. Therefore the true relationship between the ASA score and mortality in this patient population remains unclear. Previous research has suggested that the ASA score lacks sufficient discrimination for prognosis after surgery (35,54). Thus surgeons are presently left with very little in their armamentarium to counsel patients regarding post-operative risks and must rely on clinical judgment (15).

The present systematic review highlights the lack of quality research for potential prognostic factors for morbidity and mortality in this high-risk population. Importantly, none of the studies examined variables associated with post-operative LOS, post-operative quality of life, loss of independence or need for nursing home placement. Given that that many elderly patients consider quality of life to be more important than quantity of life, (16,17) research that addresses these patient-centered outcomes is needed. This issue was highlighted in a recent quality improvement guideline for optimal Preoperative Assessment of Geriatric Surgical Patients (42). Future research evaluating prognostic factors for perioperative outcomes in elderly patients should also include frailty, which has been associated with post-operative morbidity, post-operative LOS and loss of independence among elderly patients undergoing elective GI surgery. (22,55,56).

Identification of prognostic factors that can be used to create predictive models may help surgeons counsel patients regarding their post-operative risks. In addition it may also help to identify strategies to improve outcomes in this patient population (53). While factors such as patient age and co-morbidities are not modifiable, other factors such as experiencing a post-operative complication might be. In addition in trying to improve outcomes associated with emergency procedures, the potential to decrease the need for emergency surgery should be examined. Older patients with chronic conditions such as incisional hernias or biliary tract disease, who are often managed expectantly with the hope that they might not need therapy, could be the group who benefit the most from elective surgery. With the increasing proportion of elderly patients, a better understanding of the risks and the benefits associated with elective versus emergency surgery is needed for common existing conditions that can lead to acute events requiring urgent surgery.

CONCLUSIONS

The literature on prognostic factors for post-operative morbidity and mortality in elderly patients undergoing non-elective GI surgery is very limited. At present, there are no established models that can assist in predicting adverse outcomes in this group. The majority of available studies are exploratory and most of evidence is of limited quality and the results are conflicting. Given the aging population and associated future need for emergency surgery in the elderly, there is a need for high-quality research in this area.

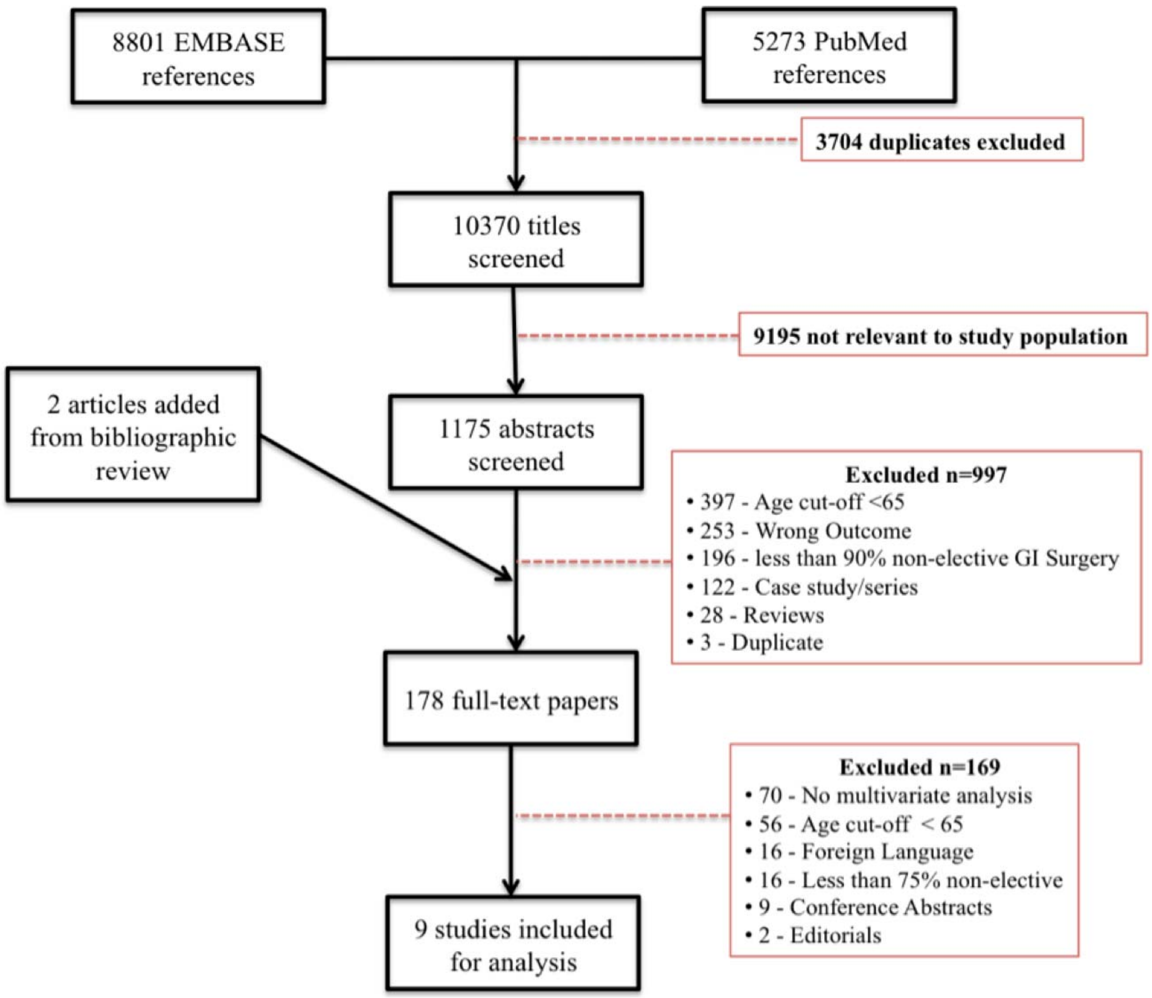

Figure 2.1 Overview of Literature Review and Study Selection

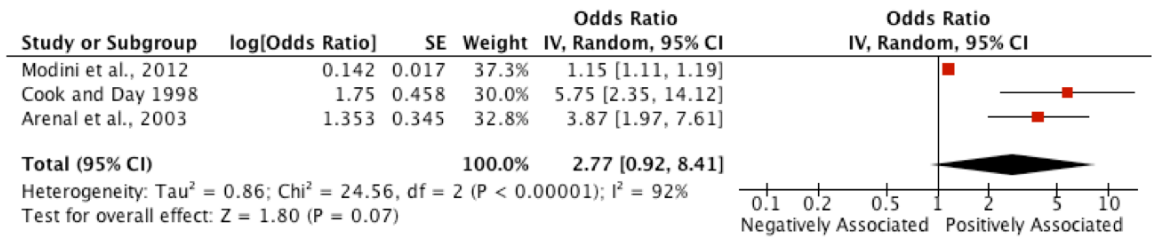

Figure 2.2 Pooled Analysis for ASA Score as a prognostic factor for post-operative mortality

Table 2.1 Study and Patient Characteristics of Included Studies

Study	Location	# of Patients	Age cut-off	Type of Surgery	Outcomes of Interest	Average age (years)	% male	Average LOS (days)	Mortality	Morbidity
Arenal et al., 2003	Valladolid, Spain	710	≥ 70	GI Surgery	In-hospital mortality	79.4	46.8	NR	21.5%	58.3%
Cook and Day, 1998	Bristol, UK	107	≥ 65	GI Surgery	In-hospital mortality	80.2	50.4	NR	43.9%	NR
Fukada et al., 2012	Kawasaki, Japan	94	≥ 80	GI Surgery	30-day mortality	85.6	38.3	NR	16.0%	43.6%
Kwok et al., 2011	Boston, USA	1358	≥ 80	Colorectal	30-day mortality	85.3	34.3	NR	28.9%	26.9%**
Leong et al., 2009	Singapore	58	≥ 80	Colorectal	30-day morbidity/mortality	83 (80-96)*	41.4	17.5 (3-108)*	27.6%	81.0%
McGillicuddy et al., 2009	New Haven, USA	292	≥ 65	Colorectal	In-hospital morbidity/ mortality	78.1	41	20.9	15.0%	34.6%
Modini et al., 2012	Rome, Italy	215	> 65	Colorectal	30-day mortality	78	47	NR	16.3%	17.2%
Okubo et al., 2008	Niigata, Japan	36	≥ 80	GI Surgery	In-hospital mortality	84 (80-97)*	44.4	38 (2-150)*	27.8%	83.3%
Vaughan-Shaw et al., 2012	Southampton, UK	88	≥ 80	GI Surgery	30-day mortality	84 (80-95)*	51.1	15 (0-72)*	33.0%	NR

*Denotes Median and Range
** Major Morbidity reported
LOS: Length of Stay; NR: Not reported

Table 2.2 Risk of Bias Assessment for Included Studies

Study	Data Acquisition	*Study Participation*	*Study Attrition*	*Prognostic Factor Measurement*	*Outcome Measurement*	*Study Confounding*	*Statistical Analysis and Presentation*
Arenal et al., 2003	Retrospective	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Cook and Day, 1998	Prospective	Low	Low	Moderate	Low	Moderate	Moderate
Fukada et al., 2012	Retrospective	Moderate	Low	Moderate	Moderate	Moderate	Moderate
Kwok et al., 2011	Prospective	Moderate	Moderate	Moderate	Low	Low	Moderate
Leong et al., 2009	Retrospective	Low	Low	Moderate	Moderate	High	Moderate
McGillicuddy et al., 2009	Retrospective	Low	Low	Moderate	Moderate	Moderate	High
Modini et al., 2012	Retrospective	Low	Low	Moderate	Low	Moderate	Low
Okubo et al., 2008	Retrospective	Low	Low	Low	Low	Low	Low
Vaughan-Shaw et al., 2012	Retrospective	Low	Low	Low	Low	Low	Low

Table 2.3 Patient Factors associated with post-operative mortality

Patient Factor	Arenal et al., 2003	Cook and Day, 1998	Fukada et al., 2012	Kwok et al., 2011	Leong et al., 2009	McGillicuddy et al., 2009	Modini et al., 2012	Okubo et al., 2008	Vaughan-Shaw et al., 2012
Age	OR=1.03 (0.97-1.09)	**OR=1.15 (1.04-1.27)**	NS	*Age < 90* **OR=0.62 (0.43-0.88)**	NS	(p=0.001)*	*Age ≥ 80* **OR=3.77 (1.32–10.7)**	NS	NS
Male Sex	OR=1.05 (0.99-1.11)	**OR=0.21 (0.19-0.23)**	NS	NS	NS	NS	NS	NS	NS
ASA Score	**OR=1.15 (1.11-1.19)**	**OR=5.88 (2.40-14.43)**	-	-	*ASA ≥ 3* **OR=10.41 (1.48-73.19)**	NS	**OR=3.87 (2.05–7.93)**	NS	NS
Presence of Comorbidities	-	NS	NS	-	-	NS	NS	NS	-
Hx of COPD	-	-	-	**OR=1.79 (1.28-2.50)**	-	-	-	-	NS
Hx of CHF	-	-	-	**OR=1.87 (1.21-2.90)**	-	-	-	-	-
Hx of Neurologic disease	-	-	-	-	-	-	**OR=4.47 (1.73–11.41)**	-	NS
ECOG Physical Status	-	-	NS	-	-	-	-	NS	-
Totally Dependent Functional Status	-	-	-	**OR=2.54 (1.88-3.43)**	-	-	-	-	-

* Data treated as continuous and no OR produced
- Prognostic factor not considered in analysis
Bold terms indicate significant difference ($p \leq 0.05$)
Bracketed values indicate 95% Confidence Intervals
NS: Not Significant

Table 2.4 Disease Factors associated with post-operative mortality

Disease Factor	Arenal et al., 2003	Cook and Day, 1998	Fukada et al., 2012	Kwok et al., 2011	Leong et al., 2009	McGillicuddy et al., 2009	Modini et al., 2012	Okubo et al., 2008	Vaughan-Shaw et al., 2012
APACHE-II Score	-	-	OR=1.13 (0.92-1.38)	-	-	-	-	-	-
POSSUM Score	-	-	*PS:* **OR=1.20 (1.03-1.42)** *OSS:* OR=1.02, (0.85-1.23)	-	-	-	-	-	-
Presence of Intestinal Obstruction	OR=1.04 (0.97-1.12)	NS	-	NS	-	-	-	-	-
Creatinine > 1.5 mg/dL		-	-	**OR=2.57 (1.97-3.36)**	-	NS	-	-	-
N/L ratio	-	-	-	-	-	-	-	-	**OR=1.03 (1.01-1.06)**
≥ 2 failing organs						-	-	**OR=5.51 (1.97-15.4)**	-
Presence of GI Bleeding	OR=1.12 (0.96-1.30)	-	-	NS	-	-	NS	-	-
Presence of Mesenteric Ischemia	**OR=1.29 (1.08-1.53)**	-	-	NS	-	-	OR=4.33 (0.89–21.11)	-	-
Presence of SIRS/Sepsis	-	NS	-	**OR=2.13 (1.60-2.82)**	-	**OR=5.26 (1.21-22.5)**	NS	-	-
Presence of Peritonitis	OR=1.04 (0.96-1.13)	-	-	-	-	-	NS	-	-
Metastatic Disease	OR=1.03 (0.91-1.17)	-	-	**OR=2.00 (1.08-3.71)**	-	-	NS	NS	-

- Prognostic factor not considered in analysis
Bold terms indicate significant difference ($p \leq 0.05$)
Bracketed values indicate 95% Confidence Intervals
NS: Not Significant
PS: Physiologic Score, OSS: Operative Severity Score

Table 2.5 Peri-operative factors associated with post-operative mortality

Peri-operative Factor	Arenal et al., 2003	Cook and Day, 1998	Fukada et al., 2012	Kwok et al., 2011	Leong et al., 2009	McGillicuddy et al., 2009	Modini et al., 2012	Okubo et al., 2008	Vaughan-Shaw et al., 2012
Duration of Symptoms prior to admission (hrs)	**OR=1.10 (1.03-1.18)**	-	*> 24 hrs of symptoms:* **OR=9.60 (1.82-50.60)**	-	-	-	-	-	-
Time from admission to OR (hrs)	OR=1.05 (0.98-1.12)	-	-	-	-	**(p=0.002)***	**NS**	**NS**	-
Time from symptom onset to OR (hrs)	OR=0.97 (0.89-1.05)	-	-	-	-	-	-	-	-
Patient adequately resuscitated	-	NS	-	-	-	-	-	-	-
EBL	-	-	-	-	-	**(p=0.02) ***	**NS**	-	-
Pre-operative Steroid use	-	-	-	**OR=0.61 (1.06-2.45)**	-	NS	-	-	-
Post-operative Complications	-	-	-	-	NS	**OR=36.17 (11.48-113.9)**	*Anastomotic leak* **OR=39.51 (5.17–301.63)**	NS	-
GI resection	OR=1.04 (0.97-1.12)	NS	-	NS	NS	-	-	-	-
Suture closure of GI perforation	OR=1.08 (0.96-1.21)	-	-	-	NS	-	-	-	-
Palliative Procedure	**OR=1.18 (1.06-1.31)**	-	-	-	-	-	-	-	-
Non-therapeutic Lap	**OR=1.26 (1.11-1.43)**	-	-	-	-	-	-	-	-
Need for Invasive Monitoring	-	**OR=6.25 (1.59-24.55)**	-	-	-	-	-	-	-
Need for ICU admission	-	**OR=11.11 (1.95-64.21)**	-	-	-	-	-	-	-
Midline laparotomy	-	-	-	-	-	-	-	-	**OR=8.86 (1.20-65.46)**

* Data treated as continuous and no OR produced
- Prognostic factor not considered in analysis
Bold terms indicate significant difference (p≤0.05)
Bracketed values indicate 95% Confidence Intervals NS: Not Significant

CHAPTER 3 IS FRAILTY ASSOCIATED WITH POST-OPERATIVE MORTALITY IN OLDER ADULTS UNDERGOING NON-ELECTIVE ABDOMINAL SURGERY? (MANUSCRIPT TWO)

ABSTRACT

BACKGROUND: Frailty is a novel prognostic factor for post-operative mortality in older adults undergoing GI surgery. This association remains to be examined in the non-elective setting. The purpose of this study is to examine the association between frailty and 90-day mortality in older adults presenting for non-elective GI surgery.

STUDY DESIGN: Patients ≥ 70 years old who underwent non-elective surgery for intra-abdominal or abdominal wall conditions between July 1, 2011 and Sept 30, 2012 were prospectively enrolled. Data were collected regarding patient demographics, frailty, treatments, and outcomes. Patients were followed for 90-days post-admission. The relationship between frailty and mortality was explored by controlling for four readily measurable pre-operative prognostic factors (age, sex, the ASA Score, and Type of Surgery) using Cox proportional hazards regression.

RESULTS: During the study period 228 patients underwent surgery (median age 77.6 years, 50.2% male). 90-day mortality was 9.6% (22 patients), and 66.2% of patients experienced a post-operative complication, of which 43.0% were major. Mortality rates increased with Frailty and ASA scores, but not age decile. In multivariate analysis frailty was not associated with 90-day mortality and the ASA score was ($p<0.0001$).

CONCLUSIONS: The ASA Score and not Frailty was not associated with 90-day mortality in this study.

INTRODUCTION

With increasing age the likelihood of undergoing non-elective (urgent or emergent) GI surgery increases (6,8,57). Non-elective surgery in older adults is associated with a 10-15 fold increase in morbidity and a 3-5 fold increase in mortality when compared to elective surgery in this age group (4,10-12). Non-elective surgery in this cohort is also associated with increased morbidity (28% vs. 10%) and mortality (15.2% vs. 2.5%) when compared to younger cohorts (13,24). This high potential for poor clinical outcomes can make treatment decisions very difficult (15). Thus, providing accurate information about treatment outcomes is an important component of patient counseling and will increasingly become so as the population ages.

Prognostic factors are often used to inform patient care (19). Previous studies have suggested that age, sex, the ASA Score, and type of surgery are potential pre-operative prognostic factors for mortality. However, the literature is limited, the majority of studies are exploratory in nature, and these associations remain to be studies further (see Manuscript #1). One novel prognostic factor for post-operative mortality is frailty. Frailty has been shown to be associated with poor outcomes in older adults undergoing elective abdominal surgery (22,23,55,56). Frailty can be defined in many ways, but the most accepted definition sees it as a state of vulnerability arising with age and undermining an organism's ability to respond to stress (21). Rockwood and colleagues have proposed measuring frailty using a Frailty Index (FI) (58,59). A FI views frailty on a continuum in relation to the accumulation of deficits where "the more things individuals have wrong with them more likely they are to be frail." (59). As such, the number of deficits a patient has is tallied and divided by the number of potential deficits in the index.

Frailty has been shown to be associated with mortality in older adults undergoing elective abdominal surgery (22), but this association remains to be examined in the non-elective setting. Therefore, the primary purpose of this study was to examine the relationship between frailty and 90-day mortality in older adults undergoing non-elective GI surgery using prospectively collected patient-level data. Second, given the paucity of literature on prognostic factors for mortality in this patient population an exploratory analysis of prognostic factors for 90-day mortality was also pursued.

METHODS

Study Population

Consecutive patients, aged 70 and older, who were admitted to an acute care surgery service at a tertiary care teaching hospital were prospectively recruited over a 15-month period (July 1, 2011-September 30, 2012). Each day, admissions to the acute care service were reviewed and patients were approached by one of the study investigators (PD or JB) to discuss the study in detail. After obtaining informed consent a Comprehensive Geriatrics Assessment (CGA) was performed in addition to a standard history and physical examination (see Appendix 4). The CGA captures several variables at baseline (two weeks prior to admission) and admission, and can be used to create a FI in a standardized manner (60). These variables include: the Katz ADL and Lawton-Brody IADL Scales, subjective information about mood, sleep and social patterns, as well as objective information related to cognitive status, strength, mobility, and balance.

Patients were eligible for inclusion in the final study cohort if they underwent non-elective surgery for an intra-abdominal or abdominal wall condition during their admission to hospital. Non-elective surgery was defined as a procedure that was not planned prior to the patient's admission to hospital. Exclusion criteria included: 1. Patients who did not undergo surgery (i.e. non-operative management of a small bowel obstruction) 2. Patients who underwent vascular surgery, urologic surgery, thoracic surgery, or surgery for skin/soft tissue infections, breast disease, or peri-anal disease. 3. Patients who underwent elective (planned) surgery, and 4. Patients who required surgery for a complication resulting from a prior elective procedure.

All medical records pertaining to the patients care were reviewed up to 90-days post-admission in order to collect information related to patient investigations, procedures performed, as well as mortality, complication, and readmission rates. Patients or their family members were contacted by telephone by one of the study investigators at 90-days post-admission to determine their status (alive or dead), and living situation. If unavailable, an attempt to contact the patient's primary care physician was also made. This study was approved by our institution's Research Ethics Board. All institutional protocols relating to database management and patient confidentiality were followed.

Frailty Measures

Two measures of frailty were examined in the study, the FI (see Appendix 5), and the CSHA Clinical Frailty Score (see Appendix 6). Both measures were assessed for each patient using the patient's baseline (defined as two weeks prior to admission) level of function. Data regarding baseline level of function were collected retrospectively from the patient and/or their caregiver at the time of admission and previous studies have suggested that measuring frailty in this manner provides a valid assessment of pre-morbid status (61).

A FI was created using elements contained in the CGA (62). Each patient's FI was scored by counting the number of deficits and dividing this count by the total number of deficits considered (52 deficits in total; see Appendix 5) (62). The CSHA Clinical Frailty Score (see Appendix Six) was devised as an easy-to-use method of assessing frailty and correlates well with the FI (63). Each patient was given a CSHA Clinical Frailty Score of 1 to 9. Similar to previous work by Rockwood et al. (63) patients were further sub-grouped as well (CSHA 1-3), pre-frail (CSHA 4), mildly frail (CSHA 5-6), frail (CSHA 6-8) and palliative (CSHA 9).

Potential Prognostic Factors

The relationship between frailty and 90-day mortality was assessed by controlling for four readily measureable pre-operative factors. These factors were determined 'a priori' and included: age at admission, sex, ASA Score (43), Operative Severity Score (56). The ASA Score was assigned by the anesthetist at the time of surgery, and if not recorded in the medical record, imputed a decision-tree induction based on the other four variables in the model. The Operative Severity Score classifies abdominal surgery into one of 3 grades: (1) superficial or laparoscopic for benign disease; (2) open, intra-abdominal for benign disease; and (3) open or laparoscopic for malignant disease.

A second group of prognostic factors were considered in an exploratory analysis. This group consisted of peri-operative factors identified from the literature as being potential prognostic factors. These were assessed based on the initial history and physical exam and/or a review of the medical record. In addition to the factors included in the 'a priori' models these included: major (Clavien III-IV, binary) and minor (Clavien I-II, binary) complications (27), BMI (kg/m2; continuous), Smoking status (never, ex-smoker, smoker; categorical), CCI (continuous) (49), the presence of mesenteric ischemia (binary), the presence of metastatic disease (binary), elevated serum creatinine (defined as greater than 120 μmol/L at admission; binary), the need for peri-operative blood products (binary), and pre-operative steroid use (binary). Morbidity was defined as any deviation from the normal post-operative course, based on a review of the medical record, and classified according to the Clavien-Dindo complication scheme (see Appendix 7). The highest Clavien complication for each patient was recorded and complications were classified as major (Clavien III-IV) or minor (Clavien I and II).

Statistical Analysis

The primary outcome of interest in the analysis was 90-day mortality. Time to death was calculated by computing the number of days between admission and death. Descriptive statistics were performed by dichotomizing patients into one of two groups, those with and without 90-day mortality. The Wilcoxon Rank Sum test was used for continuous variables, and the Fisher exact test for categorical variables. Where multiple categories existed the Mantel-Haenszel Chi-Square test was used.

For the multiple regression analysis time to death was entered into the model and patients surviving beyond 90-days post-admission were censored. Cox proportional hazards regression analysis was performed for two 'a priori' models. Factors entered into the model included: Age, Sex, ASA Score, Operative Severity Score, and either the CSHA Clinical Frailty Score (Model #1) or FI (Model #2). For the exploratory analysis simple Cox proportional hazards regression was first performed. Prognostic factors of significance (defined as $P \leq 0.10$) were then entered into the full model and multiple proportional hazards regression performed. Statistical significance was set at $P \leq 0.05$.

RESULTS

Over the study period 520 patients aged 70 and older were admitted to the acute care surgery service (see Figure 3.1). Of these 49 (9.3%) were undergoing elective surgery or were complications thereof and were excluded. 7 patients (all non-surgical) were admitted for palliative reasons and died shortly after admission before enrollment in the study. 42 patients (8.0%) did not consent. The remaining 422 patients satisfied selection criteria at admission, but only 228 of these underwent surgery representing the final study cohort (see Figure 3.1).

Patient demographics, admission diagnosis, and initial procedure performed are summarized in Tables 3.1, 3.2 and 3.3 respectively. At admission 28.1% of patients (64/228) were well (CSHA 1-3), 28.5% of patients (65/22) were pre-frail (CSHA 4), 24.6% of patients (56/228) were mildly frail (CSHA 5), 16.7% of patients (38/228) were moderate-severely frail (CSHA 6-7), and 2.2% of patients (5/228) were palliative (CSHA 9). The 90-day mortality rate was 9.6% (22/228); 59.1% (13 patients) of these patients died during the index admission, and 40.9% (9 patients) died after discharge. The causes of death included cancer, intra-abdominal bleeding, intra-abdominal sepsis, line sepsis, liver failure, respiratory failure, trauma and urosepsis (see Table 3.4). Bivariate analysis suggested that patients dying within 90-days of admission had higher CCIs (p=0.002), higher CSHA Scores (p=0.006), higher FI's (p=0.003), higher ASA scores (p=0.003), and increased rates of major morbidity (p<0.0001) than those that lived (see Table 3.1).

28.5% (65 of 228) experienced a major complication, and an additional 37.7% (86 of 228) experienced a minor complication, representing an overall complication rate of 66.2% (151 of 228). Mortality rate increased with ASA score (see Table 3.5), but not age decile (see Table 3.6).

Factors associated with 3-month mortality ('A priori' models)

When the CSHA Clinical Frailty Score was entered into the 'a priori' model only the ASA Score (HR=4.51; 95% CI: 2.37-8.60, $p<0.0001$) was associated with 90-day mortality (see Table 3.7). When the FI was entered into the 'a priori' model again only the ASA Score (HR=4.52; 95% CI: 2.40-8.53, $p<0.0001$) was associated with 90-day mortality (see Table 3.7). There was no relationship between the CSHA frailty scale score or FI and 90-day mortality.

Factors associated with 3-month mortality (exploratory models)

Simple Cox proportional hazard regression suggested that the FI ($p=0.005$), the ASA Score ($p<0.0001$), open surgery for benign disease ($p=0.04$), major complications ($p<0.0001$), the CCI ($p=0.005$), and peri-operative blood transfusion ($p=0.01$) were associated with 90-day mortality (see Table 3.8). Multiple Cox proportional hazard regression suggested that only ASA Score (HR= 3.49; 95% CI: 1.70-7.17, $p=0.007$) was associated with 90-day mortality (see Table 3.8).

DISCUSSION

This study examined 90-day mortality in older adults undergoing non-elective GI surgery. 90-day mortality was chosen as the primary outcome of interest as a recent study has suggested that a significant proportion of morbidity and mortality occur after discharge (64). Overall, the mortality rate in this study was quite low (9.6%; 22 of 228 patients), especially when in-hospital mortality was considered (5.7%; 13 of 228 patients). Previous studies of older adults undergoing non-elective abdominal surgery have suggested that in-hospital mortality rates range from 15-44% (10,36). One possible explanation for this discrepancy is heterogeneity in our patient population. This cohort included patients who were acutely ill and required emergency surgery (i.e. perforated diverticulitis) and well as patients who underwent less urgent surgery (i.e. cholecystectomy after resolution of gallstone pancreatitis). As such, some patients would not be classified as acutely ill at the time of surgery thereby reducing the overall mortality rate of the cohort.

This study is the first to explore the relationship between frailty and 90-day mortality in older adults undergoing non-elective abdominal surgery. In both 'a priori' models, as well as the exploratory analysis frailty was not associated with 90-day mortality. Although, frailty has been shown to be associated with mortality in older adults admitted to medical services (65,66), only two authors have examined the relationship between frailty and post-operative mortality in patients undergoing abdominal surgery (22,56). In 2009, Robinson et al., examined the relationship between clinical markers of frailty and 6-month mortality, and found that six markers of frailty were associated with this outcome in older adults undergoing elective abdominal surgery (22). In contrast, Saxton and Velanovich examined the relationship between a FI and 30-

day mortality in older adults undergoing elective abdominal surgery and found no relationship between frailty and 30-day mortality (56).

There are four possible reasons why our study failed to show an association between frailty and post-operative mortality. First and foremost, it is possible that frailty is not associated with mortality in this patient population and that other factors such as the patient's current physical state (i.e. illness severity) are more important than how frail someone is. This is supported by our results in that only the ASA Score was associated with 90-day mortality. Second, our study focused exclusively on patients undergoing abdominal surgery while Robinson's study-included patients undergoing vascular, thoracic, and urological procedures. As such, the effect of frailty may vary by depending on the cohort make-up. Third, the Robinson study sought to create a frailty index for surgical patients and did not adjust for other factors including the ASA score. It is therefore possible that the association would not remain on a more extensive multiple regression analysis. Lastly, frailty can be measured in many ways and it is possible that another measure of frailty may have been better to suited. From the geriatric literature, the other predominant approach to measuring frailty has been proposed by Fried et al., who suggest an operational definition of frailty based on the presence or absence of the following indicators: 1. Unintentional weight loss, 2. Slow walking speed, 3. Subjective exhaustion, 4. Low grip strength, and 5. Low levels of physical activity (67). Fried's index has been shown to be associated with length of stay (LOS), complications, and discharge to institution in elderly adults undergoing non-elective abdominal surgery but not mortality (55). However, the applicability of this measure in the acute setting, is called into question, as acute illness can affect the measurement of these variables (21,60).

In the present study only the ASA Score was associated with mortality in both the 'a priori' and exploratory models. Although relatively few mortalities occurred, and there is a possibility of model saturation, this result is supported by several other studies showing an association between ASA and mortality in this patient population (10,20,34,37). With respect to the other factors in the 'a priori' model no previous study has examined the OSS in this patient population and our results suggest no association with mortality. Further, we did not see an association between age and mortality, and although some studies have suggested that age is associated with mortality in this patient population (10,35-37), there is equal evidence to suggest that age is not associated with this outcome (20,33,34,38,39). Lastly, with respect to sex only one study has suggested that male sex is protective against mortality in this patient population (10), while eight others suggest no association (20,33-39). As we did not see evidence of this association our results would support these latter studies suggesting that the former study was a spurious result.

Limitations of the study

There are several limitations associated with the present study. First, the overall mortality rate was low (9.6%), and the number of outcomes was small (22 in this study). As a general rule 1 predictor variable is considered for 10 outcomes and there is a possibility that both the 'a priori' and exploratory models were saturated. However, collecting prospective high quality data is time consuming and labor intensive and it can be difficult to assemble a large cohort. Second, it is possible that some degree of selection bias may have been present. We noted that no patient received a CSHA clinical frailty score of eight. In general these patients are considered quite ill at baseline and mortality rates from a minor illness such as a cold would be high. As such, the most-frail patients did not present to our attention. That said, given the very low non-consent rate we feel that the study population is reflective of the older adult population presenting to an acute care surgery service. Selection bias may also have occurred, as the most frail and sick patients may not have been offered surgery. However our institution does not have a policy of refusing surgery based on these grounds and we expect that the overall number of patients in this group would be small. Further, this would tend to have biased the results towards the null. Finally, measurement bias may have operated as frailty was scored by two observers and intra-observer reliability was not assessed. However, unpublished work by Rockwood et al., has suggested that the intra-observer reliability of the FI is good (k=0.76). Further, any variability in measurement would represent real use of the tool and overall we feel that this bias, while tending to bias towards the null, would be negligible.

CONCLUSIONS

The ASA Score was the only factor associated with mortality in the present study. Frailty was not associated with mortality this patient population.

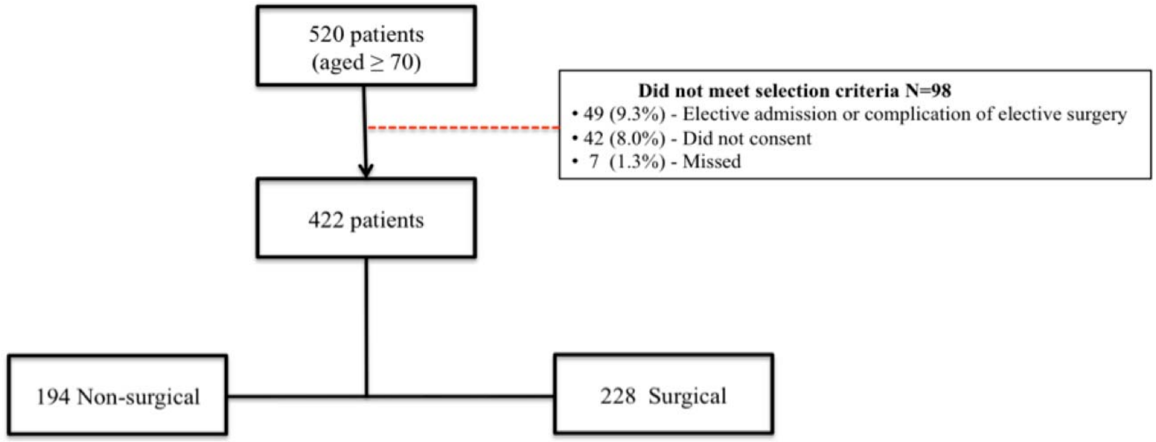

Figure 3.1 Overview of Patients admitted to the acute care surgery service (July 1, 2011-September 30, 2012)

Table 3.1 Characteristics of patients alive and dead at 90-days post-admission

	Alive (N=206)	Dead (N=22)	P-value
Age (years; mean, SD)	78.5 (5.5)	79.1 (5.6)	0.53
Male (N, %)	100 (48.5)	13 (59.1)	0.38
BMI (kg/m^2; mean, SD)	25.9 (5.1)	25.5 (4.7)	0.60
CCI (mean, SD)	1.5 (1.8)	2.9 (2.2)	**0.002**
CSHA Score (mean, SD)	4.3 (1.3)	5.2 (1.5)	**0.006**
FI (mean, SD)	0.18 (0.09)	0.23 (0.08)	**0.003**
ASA Score (mean, SD)	2.5 (0.6)	3.3 (0.9)	**0.003**
Current smoker (N, %)	26 (12.8)	6 (27.3)	0.14
Operative Severity Score			
Grade 1	76 (37.1)	3 (13.6)	
Grade 2	102 (49.8)	15 (68.2)	
Grade 3	27 (13.2)	4 (18.2)	0.06*
Complications			
Major (Clavien III-IV)	45 (21.8)	20 (90.9)	**<0.0001**
Minor (Clavien I-II)	84 (40.8)	2 (9.1)	**0.003**
Length of Stay (days; mean, SD)	11.3 (33.6)	15.8 (18.9)	0.68
In-hospital mortality (N, %)	0 (0)	13 (59.1)	-

**Chi-Square test for trend*

Table 3.2 Admission Diagnosis of the study cohort (Surgical Patients)

Reason for Admission	Number
Small Bowel Obstruction	67
Acute Cholecystitis	38
Large Bowel Obstruction	25
Incarcerated Hernia	20
Gallstone Pancreatitis	16
Acute Diverticulitis	13
Biliary Obstruction	12
Acute Appendicitis	8
GI Bleed	8
Peptic Ulcer	7
Trauma	5
Ischemic Colitis	4
Ischemic Bowel	3
Other	2

Table 3.3 Initial procedures performed

Procedure	Number
Bowel Resection (N=68)	
Small	27
Right Colon	19
Left Colon	4
Sigmoid Colon	11
Subtotal Colectomy	7
Cholecystectomy (N=61)	
Lap	42
Open	19
Hernia Repair (N=34)	
Groin	16
Ventral	17
Parastomal	1
Lysis of Adhesions	28
Appendectomy (N=11)	
Lap	7
Open	4
Stoma (N=11)	
Loop Colostomy	6
Loop Ileostomy	5
Laparotomy	6
Drainage of Intra-abdominal Abscess	2
Splenectomy	1

Table 3.4 Cause of Death (N=22)

Cause of Death	Number
Cancer	3
Intra-abdominal Bleeding	2
Intra-abdominal Sepsis	7
Line Sepsis	1
Hepatic Decompensation	1
Respiratory Failure/Pneumonia	4
Trauma	1
Urosepsis	1
Unknown	2

Table 3.5 Mortality rate by ASA Score

ASA Score	Mortality (N,%)
I	0/5 (0)
II	1/83 (1.2%)
III	9/107 (8.4%)
IV	9/26 (34.6%)
V	2/3 (66.7%)

Table 3.6 Mortality rate by Decade

Age Group	Mortality (N,%)
70-79	13/152 (8.6%)
80-89	9/64 (14.5%)
90+	0/14 (0)

Table 3.7 'A priori' Cox proportional hazards models for 90-day mortality

	Model #1 (HR; 95% CI)	**Model #2 (HR; 95% CI)**
Age (per yr increase)	1.01 (0.92-1.10) p=0.88	1.01 (0.93-1.10) p=0.85
Female Sex	0.47 (0.19-1.19) p=0.11	0.45 (0.18-1.13) p=0.09
CSHA		
1-3	1 (ref)	-
4	1.83 (0.34-9.84) p=0.48	-
5	2.40 (0.48-11.91) p=0.29	-
6-8	2.29 (0.41-12.78) p=0.35	-
9	2.47 (0.22-28.02) p=0.47	-
FI (per 0.01 increase)	-	1.03 (0.99-1.08) p=0.15
ASA	**4.51 (2.37-8.60) p<0.0001**	**4.52 (2.40-8.53) p<0.0001**
Operative Severity		
Grade 1	1 (ref)	1 (ref)
Grade 2	1.73 (0.47-6.44) p=0.41	1.86 (0.50-6.87) p=0.35
Grade 3	2.23 (0.48-10.42) p=0.31	2.39 (0.52-10.94) p=0.26

Table 3.8 Exploratory Cox proportional hazards models for 90-day mortality

Prognostic Factor	Simple Regression (HR; 95 % CI)	Multiple Regression (HR; 95 % CI)
Age (per yr increase)	1.02 (0.95-1.10) p=0.60	-
Female Sex	0.69 (0.29-1.60) p=0.38	-
FI (per 0.01 increase)	**1.06 (1.02-1.10) p=0.005**	1.03 (0.98-1.08) p=0.21
ASA Score	**4.72 (2.75-8.08) p<0.0001**	**3.49 (1.70-7.17) p=0.007**
Operative Severity		
Grade 1	1 (ref)	1 (ref)
Grade 2	**3.57 (1.03-12.32) p=0.04**	0.79 (0.19-3.26) p=0.74
Grade 3	3.48 (0.80-16.01) p=0.09	1.46 (0.29-7.30) p=0.65
Complications		
Major	**30.09 (7.03-128.84) p<0.0001**	9213611 (0 - ∞) p=0.99
Minor	**0.15 (0.04-0.66) p=0.01**	771816.5 (0 - ∞) p=0.99
BMI (per kg/m^2 increase)	0.99 (0.90-1.08) p= 0.75	-
Smoking Status		
Non-smoker	1 (ref)	1 (ref)
Ex-smoker	1.33 (0.45-3.98) p=0.60	0.94 (0.27-3.32) p=0.93
Smoker	2.85 (0.87-9.35) p=0.08	1.60 (0.42-6.06) p=0.49
CCI (per 1 unit increase)	**1.26 (1.09-1.47) p=0.003**	1.05 (0.84-1.31) p=0.67
Mesenteric Ischemia	4.92 (0.66-36.58) p=0.12	-
Presence of Metastatic Disease	2.27 (0.53-9.73) p=0.27	-
Serum Creatinine ≥ 120 μmol/L	**2.29 (0.98-5.36) p=0.06**	0.66 (0.22-2.08) p=0.48
Blood transfusion	**6.53 (1.52-28.04) p=0.01**	6.05 (0.64-65.93) p=0.11
Pre-operative Steroid use	1.76 (0.41-7.54) p=0.44	-

CHAPTER 4 LOSS OF INDEPENDENCE AND INSTITUTIONALIZATION AFTER NON-ELECTIVE ABDOMINAL SURGERY IN OLDER ADULTS (MANUSCRIPT THREE)

ABSTRACT

BACKGROUND: Non-elective abdominal surgery in older adults often results in a functional decline leading to temporary (or permanent) discharge to institution. Discharge to insitution is an important issue as it significantly reduces patient quality of life and results in increased financial burden for the health care system. To our knowledge no study has examined prognostic factors for this outcome in this patient population. The purpose of this study is to examine the association between pre-operative prognostic factors and discharge to institution in older adults presenting for non-elective abdominal surgery.

STUDY DESIGN: Consecutive patients aged ≥ 70 admitted to an acute surgery service were prospectively enrolled over a 15-month period. At admission, a standard history and physical examination was performed as well as a comprehensive geriatrics assesment. Patients were followed for 90-days post-admission and descriptive statistics were performed for those discharged home and to institution. An 'a priori' model for discharge to institution was proposed using five pre-operative prognostic factors including: age, sex, a frailty measure (Frailty Index or CSHA Clinical Frailty Score), the ASA Score, and Type of Surgery, and multiple logistic regression performed.

RESULTS: In all 197 were community dwellers surviving to discharge underwent surgery. Of these 44 (22.3%) required discharge to institution. In the 'a priori' models the ASA Score, open surgery for benign disease, the CSHA Clinical Frailty Score and the Frailty Index were independently associated with discharge to institution.

CONCLUSIONS: Pre-operative factors are associated with discharge to institution and could be used to stratify patients for pre-operative counseling and resource planning.

INTRODUCTION

The Canadian population is aging, and it is estimated that by the year 2050 fully one in four Canadians will be over the age of 65 (1). As highlighted by the National Hospital Discharge Survey the aging population is putting increasing strain on the health care system, as the proportion of discharged patients over the age of 65 has increased from 10% in 1970, to 37% in 2007 (68,69). This trend has had an impact on general surgical services more than any other discipline (42), as older adults undergo abdominal surgery at disproportionate rates (5,6), and a large proportion (40%) of these procedures occur on a non-elective (urgent or emergent) basis (6,8).

Non-elective abdominal surgery in older adults may lead to a functional decline (70), and loss of independence. This results in temporary institutionalization in 20-30% of patients and has been associated with a significant negative impact on patient quality of life (23,71,72), as well as increased health care costs for an already stressed system (23,70). However, loss of independence does not necessarily require institutionalization and some patients can return to living in the community but can no longer live alone. The extent to which this occurs among elderly patients undergoing non-elective abdominal surgery and its impact on quality of life is unknown.

The ability to predict loss of independence and the need for institutionalization after non-elective abdominal surgery would be useful for patient counseling, discharge planning, and resource allocation. In order to develop such predictive tools an understanding of the factors associated with loss of independence and institutionalization is required. Furthermore, identification of factors associated with institutionalization may lead to strategies to prevent this outcome in elderly patients. Unfortunately, very little research has examined prognostic factors for institutionalization after non-elective surgery in elderly patients. Presently there are no tools available to predict this in s this outcome in surgical patients.

The purpose of this study was to determine the impact of non-elective abdominal surgery on independence and living situation of patients ≥ 70 years old, and to examine which factors are associated with discharge to institution in this patient cohort.

METHODS

Study Population

Consecutive patients admitted to a tertiary hospital acute care surgery service were prospectively recruited over a 15-month period (July 1, 2011-September 30, 2012). Each day, admissions to the acute care service were reviewed and patients satisfying selection criteria were approached by one of the study investigators (PD or JB). After obtaining informed consent a Comprehensive Geriatrics Assessment (CGA; see Appendix 4) was performed in addition to a standard history and physical examination. The living status prior to admission was determined for each patient. Patients were categorized as 'community dwellers' (those living alone or with others) or 'institutionalized' (those living in a Lodge, nursing home, or hospitalized for > 2 weeks).

Inclusion criteria

1. All patients, aged 70 and older, admitted, regardless of route (via ER, family physician's office, or in-patient consult), to the acute care surgery service.

Exclusion criteria

1. Patients without intra-abdominal or abdominal wall pathology including: head and neck pathology, vascular pathology, urologic pathology, thoracic pathology, skin and soft tissue infections, breast pathology, and peri-anal disease
2. Patients not undergoing surgery
3. Patients admitted from an institution (nursing home, Lodge, in-patient for ≥ 2 weeks)
4. Surgical patients dying in hospital
5. Patients undergoing elective (planned) surgery.
6. Patients who require treatment for a complication resulting from a prior elective procedure.

All medical records pertaining to the patients care were reviewed up to 90-days post-admission in order to assess treatments, complications, and readmission rates. Patients or their family members were contacted by phone by one of the study investigators at 90-days post-admission to determine their status (alive or dead), and living situation. This study was approved by the CDHA Research Ethics Board. All institutional protocols relating to database management and patient confidentiality were followed.

Outcome Variables

The primary outcomes of interest were loss of independence and discharge to institution. The living status for each patient at discharge from hospital and at 3 months after admission was determined. At each time point patients were categorized as living alone, living with others, or living in an institution. Institutionalization was defined as a nursing home, a skilled nursing facility (Lodge), home hospital, or a rehabilitation center. Loss of independence was defined as failure to return to pre-admission living status.

Potential Predictor Variables

The relationship between five pre-operative factors selected 'a priori' (age at admission, Sex, ASA Score (43), Operative Severity Score (56), and one of two frailty measures (Frailty Index (FI) or Canadian Study of Health and Aging (CSHA) Clinical Frailty Score) and discharge to institution was examined. The ASA Score was assigned by the anesthetist at the time of surgery, and if not recorded in the medical record, imputed using multiple imputation techniques based on the other four variables in the model. The Operative Severity Score classifies abdominal surgery into one of 3 grades: (1) superficial or laparoscopic for benign disease; (2) open, intra-abdominal for benign disease; and (3) open or laparoscopic for malignant disease. Both measures of frailty were assessed using the patient's baseline (defined as two weeks prior to admission) level of function. This information was collected at the time of enrollment into the study.

Data regarding baseline level of function were collected retrospectively from the patient and/or their caregiver, and previous studies have suggested that measuring frailty in this manner provides a valid assessment of pre-morbid status (61). A FI was created using elements contained in the CGA (62). Each patient's FI was scored by counting the number of deficits and dividing this count by the total number of deficits considered (52 deficits in total; see Appendix 5) (62). For the CSHA Clinical Frailty Score each patient was given a CSHA Clinical Frailty Score of 1 to 9 (See Appendix 6). Patients were further sub-categorized as well (CSHA 1-3), pre-frail (CSHA 4), mildly frail (CSHA 5), frail (CSHA 6-7), or palliative (CSHA 9).

A second group of prognostic factors were considered in an exploratory analysis. This group consisted of peri-operative factors identified from the literature as being potential prognostic factors for mortality. In addition to the factors included in the 'a priori' models and were assessed based on the initial history and physical exam and/or a review of the medical record. These factors included: major (Clavien III-IV; see Appendix 7, binary) and minor (Clavien I-II, binary) complications (27), BMI (kg/m2; continuous), Smoking status (never, ex-smoker, smoker; categorical), CCI (continuous) (49), the presence of mesenteric ischemia (binary), the presence of metastatic disease (binary), elevated serum creatinine (defined as greater than 120 μmol/L at admission; binary), the need for peri-operative blood products (binary), and pre-operative steroid use (binary).

Statistical Analysis

Statistical analysis was performed using the Wilcoxon Rank Sum test for continuous variables and using Fischer's exact test for categorical variables. Where multiple categories existed the Mantel-Haenszel Chi-Square test was used. Statistical analysis compared characteristics of subjects discharged home and to institution. Logistic regression analysis was performed to examine the relationship between the five peri-operative factors (Age, Sex, ASA Score, Operative Severity Score, and either the CSHA Clinical Frailty Score (Model #1) or FI (Model #2) and discharge to institution. For the exploratory analysis simple logistic regression was first performed. Prognostic factors of significance (defined as $P \leq 0.10$) were then entered into the full model and multiple logistic regression performed. Statistical significance was set at $P \leq 0.05$.

RESULTS

Patient Demographics

Over the study period 422 patients satisfied selection criteria, of which 228 underwent non-elective GI surgery (see Figure 3.1). Of these 18 (of 228) patients were admitted from an institution (10 Lodge, 7 nursing home, 1 hospitalized ≥ 2 weeks) and 13 (of 228) patients died during the index admission leaving a final study cohort of 197 community dwellers (see Table 4.1). Characteristics of patients discharged home and to an institution are summarized in Table 4.1. Patients discharged to an institution tended to have higher CCI's ($p=0.0004$), higher CSHA Clinical Frailty Scores ($p<0.0001$), higher FI's ($p<0.0001$), and higher ASA scores ($p<0.0001$). Further, patients discharged to institution were more likely to have undergone laparotomy ($p<0.0001$), suffered major complications more frequently ($p<0.0001$), and had longer length of stays ($p<0.0001$). Of note, patients discharged to the community were more likely (18.9% vs. 7.6%; $p=0.02$) to be readmitted to hospital within 90-days of admission.

At admission the majority of patients (70.1%, 138 patients) were living with others and the remainder (29.9%; 59 patients) were living alone (see Table 4.2). The most common diagnoses were biliary tract disease and small bowel obstruction (see Table 4.3), and the most common procedures performed were cholecystectomy and bowel resection (see Table 4.4).

At the time of discharge from hospital 71.6% (141 patients) of patients returned to their pre-admission living situation, 6.1% (12 patients) required additional supports, and 22.3% (44 patients) required institutionalization at discharge (see Table 4.2). Patients discharged to an institution waited an average of 6.7 ± 10.7 days for an institutional bed once 'medically ready' for discharge. Three months following discharge 75.1% had returned to their pre-admission living situation, 3.6% (7 patients) had died, and 16.8% experienced a loss of independence (see Tables 4.5 and 4.6). Of the 44 patients who had been discharged to an institution 19/44 (43.2%) remained in an institution at 3-month follow-up (see Table 4.5), while only 4/153 (2.6%) of those discharged to the community were institutionalized at this time point (see Table 4.6).

Factors associated with Discharge to Institution

On multivariate analysis, using the factors selected 'a priori', frailty (higher CSHA Clinical Frailty Scores (OR=1.45; 95%CI 1.06-1.98, p=0.02), higher frailty index (OR=1.07; 95%CI 1.02-1.13 p=0.006)), increasing ASA Score (OR=2.65; 95%CI 1.42-4.90, p=0.002), and laparotomy for benign disease (OR=10.22, 95%CI: 2.24-46.68, p=0.01), were associated with discharge to institution (see Table 4.7) In the exploratory model (see Table 4.8) simple logistic regression revealed that age (p=0.01), the FI (p<0.0001), the ASA Score (p<0.0001), open surgery for benign (p=0.005) and malignant (p=0.005) disease, major complications (P<0.0001), BMI (p=0.02), the CCI (p=0.02), serum creatinine ≥ 120 μmol/L at admission (p=0.002), and pre-operative steroid use (p=0.04) were associated with discharge to institution. On Multiple logistic regression increasing FI (OR= 1.08; 95% CI: 1.03-1.14; p=0.004), increasing ASA Score (OR= 2.08; 95% CI: 1.01-4.28; p=0.05), surgery for malignant disease (OR= 9.27; 95% CI: 1.46-58.98; p=0.05), major complication (OR= 3.37; 95% CI: 1.26-9.01; p=0.02), and an admission serum creatinine ≥ 120 μmol/L (OR= 3.10; 95% CI: 1.04-9.25; p=0.04), were associated with discharge to institution.

DISCUSSION

Institutional placement after hospitalization is an important issue for both the heatlh care system and patient. First, from the system's perspective, the demand for nursing home and rehabilitation resources typically exceeds the supply of beds (23,70), and patients often remain in acute care beds for extended periods of time. In our study, patients discharged to an institution waited an average of 6.7 days after being medically ready for institutional placement. This "bed-blocking" ties up acute care resources and contributes to increased wait times for patients needing elective surgery (73). Second, from the patient's perspective institutional placement as a result of a functional decline often results in decreased quality of life for patients (72). This is especially concerning as the majority of older adults consider quality of life to be as important as its quantity (16,17). Furthermore, if sustained, this loss of functional independence, is associated with high 6-month mortality rates as many patients continue to decline (71,72).

In the present study 22.3% of patients who had been living in the community were discharged to an institution after undergoing non-elective abdominal surgery. This result is consistent with previous research which had reported an initial discharge to institution rate in older adults between 20 and 30% (23,70). However the need for ongoing institutionalization or the potential for functional improvement after initial discharge has not been well studied (23,74,75). Almost half of the patients who were discharged to an institution in the present study had returned to community living by 3 months after admission. This potential for improvement after initial institutionalization highlights the need for adequate rehabilitation resources and appropriate selection of patients to receive these services.

Several factors were associated with discharge to institution in this study including ASA score, frailty, operative severity and major complications. Increasing ASA score has been associated with morbidity and mortality in elderly patients undergoing non-elective abdominal surgery, but its relationship with discharge to institution has not been previously studied. Frailty is a relatively novel prognostic factor that has been associated discharge to institution in medical (76) and elective surgical patients (23). Frailty, which has been defined as a lack of physiologic reserve, was measured using two separate measures of frailty. The CSHA Clinical Frailty Score was devised as an easy-to-use method of assessing frailty and correlates well with the FI (63). Both the ASA score and the CSHA clinical frailty score can be quickly determined pre-operatively at the patient bedside and could be easily implemented into clinical practice (76). The identification of such pre-operative factors could assist with pre-operative counseling and the development of predictive models to determine the need for institutionalization. This would have implications for patient counseling, bed management, discharge planning and resource allocation.

Patients who experienced major complications were more likely to require institutionalization. While pre-operative factors such as ASA score or frailty cannot be modified in an emergency setting, it may be possible to prevent or mitigate the consequences of major complications and improve patient outcomes. Indeed, preventing complications is the major focus of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) which aims to reduce complications and in turn reduce patient mortality as well as the need for institutional placement (77).

While most previous research of outcomes after non-elective abdominal surgery has focused on institutionalization, loss of independence can also impact patients who return to living in the community. Of those patients who had been living alone prior to admission and were discharged back into the community, only 73% were able to return to independent living. Of those still living in the community three months following admission independent living had only increased to 77%. How this may impact patient quality of life or that of the individuals who live with the patient is unknown.

There are several limitations associated with this study. First the number of outcomes is small (44 patients). As a general rule 1 predictor variable is considered for 10 outcomes and there is a possibility that both the ‘a priori’ and exploratory models were saturated. This may explain why surgery for malignant disease was not associated with discharge to institution in the ‘a priori’ models. Second, there may have been a small selection bias operating, as the most frail and sick patients may not have made it into the hospital. Indeed, we noted that no patient in our study received a CSHA clinical frailty score of 8. In general these patients are considered quite ill at baseline and mortality rates from a minor illness such as a cold would be high. As such, the frailest patients did not present to our attention. That said, given the very low non-consent rate we feel that the study population is reflective of the older adult population presenting to an acute care surgery service. In addition, these patients would tend to have been institutionalized at baseline and therefore would have been excluded from our analysis. Second, selection bias may also have operated, as the most frail and sick patients may not have been offered surgery. Our institution however does not have a policy of refusing surgery based on these grounds and we expect that the overall number of patients in this group would be small. Further, this would tend to have biased the results towards the null. Lastly, a small amount of measurement bias may have operated as patients or their family members were asked to provide information on their baseline (defined as two weeks prior to admission) level of function. In general we feel that this bias would be small as most people are able to recall their recent level of function and as measuring level of function in this manner has been shown to be a valid method of assessing frailty (61).

CONCLUSION

Non-elective abdominal surgery in elderly patients is associated with loss of independence leading to institutionalization and loss of independent living among those who are discharged back to community living. Increasing frailty, ASA score and major complications were associated with institutionalization in this patient cohort. Further research is needed to better understand the risk factors for institutionalization as the need for such services will continue to grow as the population ages.

Table 4.1 Characteristics of Patients Discharged home and to an institution

	Discharged home (N=153)	Discharged to an institution (N=44)	P-value
Age (years; mean, SD)	77.6 (4.8)	80.1 (7.1)	0.10
Male (N, %)	78 (51.0)	24 (54.6)	0.73
BMI (kg/m^2; mean, SD)	26.4 (5.0)	24.4 (4.5)	0.06
CCI (mean, SD)	1.4 (1.8)	2.1 (2.0)	**0.004**
CSHA Score (mean, SD)	4.0 (1.2)	5.1 (1.4)	**<0.0001**
FI (mean, SD)	0.15 (0.07)	0.23 (0.09)	**<0.0001**
ASA Score (mean, SD)	2.4 (0.6)	3.0 (0.4)	**<0.0001**
Current smoker (N, %)	19 (12.5)	9 (20.5)	0.18
Operative Severity Score			
Grade 1	66 (41.7)	2 (18.9)	
Grade 2	68 (46.4)	32 (60.4)	
Grade 3	18 (11.9)	10 (20.8)	**<0.0001**
Complications (N,%)			
Major	26 (17.0)	23 (52.2)	**<0.0001**
Minor	59 (38.6)	17 (38.6)	0.99
Length of Stay (days; mean, SD)	7.2 (24.3)	25.0 (54.5)	**<0.0001**
Readmission (N,%)	32 (18.9)	4 (7.6)	**0.02**

Table 4.2 Pre- and post-admission living situation of 'community dwelling' surgical patients

	Discharge Destination				
	Living Alone (N,%)	Living with others (N,%)	Living in a Lodge (N,%)	Nursing Home (N,%)	PCU/ Restorative (N,%)
Living Alone (N=59)	32 (51.6)	12 (19.4)	**1 (1.6)**	**2 (3.2)**	**12 (19.4)**
Living with others (N=138)	3 (2.0)	106 (71.6)	-	-	**29 (19.6)**

***** Bolded cells represent patients moving from the community to an institution

Table 4.3 Admission Diagnosis of 'Community Dwelling' Patients

Reason for Admission	Number
Small Bowel Obstruction	54
Acute Cholecystitis	35
Large Bowel Obstruction	22
Incarcerated Hernia	16
Gallstone Pancreatitis	12
Bilary Obstruction	11
Acute Diverticulitis	10
GI Bleed (N=8)	
Lower	5
Upper	3
Acute Appendicitis	8
Other	7
Ischemic Bowel	5
Ischemic Colitis	4
Peptic Ulcer	3
Trauma	2

Table 4.4 Initial Procedure Performed

Procedure	Number
Appendectomy	
Lap	7
Open	4
Bowel Resection	
Small	27
Right Colon	22
Left Colon	4
Sigmoid Colon	8
Subtotal Colectomy	7
Cholecystectomy	
Lap	42
Open	19
Drainage of Intra-abdominal Abscess	2
Hernia Repair	
Groin	16
Ventral	17
Parastomal	1
Laparotomy	6
Lysis of Adhesions	28
Splenectomy	1
Stoma	
Loop Colostomy	6
Loop Ileostomy	4

Table 4.5 3-month living situation of patients discharged to an institution

	3-month living situation						
	Living Alone (N,%)	Living with others (N,%)	Living in a Lodge (N,%)	Nursing Home (N,%)	Deceased (N,%)	In-patient (N,%)	Total (N)
Living Alone	-	3 (20.0)	**3 (20.0)**	**2 (13.3)**	1 (6.7)	**6 (40.0)**	15
Living with others	1 (3.4)	16 (55.1)	-	**4 (13.8)**	4 (13.8)	**4 (13.8)**	29

***** *Bolded cells represent patients moving from the community to an institution*

Table 4.6 3-month living situation of patients discharged home

	3-month living situation						
	Living Alone (N,%)	Living with others (N,%)	Living in a Lodge (N,%)	Deceased (N,%)	In-patient (N,%)	Lost to F/U (N,%)	Total (N)
Living Alone	33 (75.0)	7 (15.9)	**1 (2.3)**	-	**1 (2.3)**	2 (4.5)	44
Living with others	3 (2.8)	99 (90.8)	-	3 (2.8)	**2 (1.8)**	2 (1.8)	109

*** *Bolded cells represent patients moving from the community to an institution*

Table 4.7 'A priori' models for Discharge to Institution

	Model #1 (OR; 95% CI)	Model #2 (OR; 95% CI)
Age (per yr increase)	1.06 (0.99-1.13) p=0.10	1.07 (0.996-1.14) p=0.06
Female Sex	0.55 (0.24-1.26) p=0.21	0.45 (0.19-1.05) p=0.06
CSHA	**1.45 (1.06-1.98) p=0.02**	-
FI (per 0.01 increase)	-	**1.07 (1.02-1.13) p=0.006**
ASA	**2.65 (1.42-4.90) p=0.002**	**2.68 (1.42-5.07) p=0.002**
Operative Severity		
Grade 1	1 (ref)	1 (ref)
Grade 2	**10.22 (2.24-46.68) p=0.01**	**8.14 (1.75-37.91) p=0.05**
Grade 3	9.88 (1.79-54.67) p=0.06	9.01 (1.62-50.28) p=0.06

Table 4.8 Exploratory model for Discharge to Institution

Prognostic Factor	Simple Regression (OR; 95 % CI)	Multiple Regression (OR; 95 % CI)
Age (per yr increase)	**1.08 (1.02-1.14) p=0.01**	1.06 (0.98-1.15) p=0.13
Female Sex	0.87 (0.44-1.70) p=0.68	-
FI (per 0.01 increase)	**1.12 (1.07-1.17) p<0.0001**	**1.08 (1.03-1.14) p=0.004**
ASA Score	**4.16 (2.32-7.44) p<0.0001**	**2.08 (1.01-4.28) p=0.05**
Operative Severity		
Grade 1	1 (ref)	1 (ref)
Grade 2	**15.53 (3.58-67.42) p=0.005**	6.07 (1.22-30.31) p=0.19
Grade 3	**18.33 (3.68-91.27) p=0.005**	**9.27 (1.46-58.98) p=0.05**
Minor Complication	1.00 (0.50-2.00) p=0.99	-
Major Complication	**5.35 (2.59-11.06) p<0.0001**	**3.37 (1.26-9.01) p=0.02**
BMI (per kg/m^2 increase)	**0.91 (0.84-0.99) p=0.02**	0.93 (0.84-1.03) p=0.16
Smoking Status		
Non-smoker	1 (ref)	-
Ex-smoker	1.17 (0.52-2.61) p=0.55	-
Smoker	2.09 (0.76-5.75) p=0.14	-
CCI (per 1 unit increase)	**1.20 (1.02-1.42) p=0.02**	0.83 (0.65-1.05) p=0.12
Mesenteric Ischemia	>999.99 (<0.001->999.99) p=0.99	-
Presence of Metastatic Disease	1.79 (0.43-6.40) p=0.42	-
Serum Creatinine ≥ 120 μmol/L	**3.09 (1.49-3.08) p=0.002**	**3.10 (1.04-9.25) p=0.04**
Blood transfusion	>999.99 (<0.001->999.99) p=0.98	-
Pre-operative Steroid use	**3.80 (1.05-13.77) p=0.04**	2.22 (0.39-12.68) p=0.37

CHAPTER 5 CONCLUSIONS

The Canadian population continues to age at an alarming rate (1). This trend will have implications for the way in which health care is to be delivered. Further, if unchecked, this will continue to stress our ability to pay for universal health services and outcome driven care will become increasingly commonplace (2). This in turn will necessitate the need for better methods of assessing medical risk as current risk assessment tools remain inadequate for this task (18). If not, in the future, as in the past, the majority of health care decisions will be based on a combination of the surgeon's experience and the patient's expectations (15). This situation can lead to a negative cycle where increasing levels of care are offered as it is often difficult to withhold further care once the initial decision to operate is made (78), leading to increased health care costs and unnecessary suffering for the patient and their families. If it was possible identify patients who are likely to experience poor outcomes (high mortality, discharge to institution) then some patients may decide to refuse care. Additionally such information may facilitate decisions to withdraw care earlier in the course of treatment if things are not going well.

Unfortunately, current methods of predicting health outcomes in the older adults undergoing non-elective surgery are inadequate (18). Although, fairly powerful risk assessment models such as the ACS-NSQIP are being developed (79), these models require information that is available post-operatively and help little with pre-operative decision making. The development of adequate (accurate, reliable, and easy-to-use) pre-operative risk assessment models requires a thorough understanding of the prognostic factors associated with poor outcomes (19). However very few studies have addressed this issue and the literature on prognostic factors for post-operative outcomes in older adults undergoing non-elective abdominal surgery remains in its infancy. Only nine studies examined prognostic factors for mortality, and two studies examined prognostic factors for complications. Further, no study considered prognostic factors for patient centered outcomes (discharge to institution or length of stay).

Given that mortality and discharge to institution are arguably the most important clinical outcomes to older patients (16,17) we examined the association between five pre-operative factors and these outcomes. The ASA Score was the only factor associated with mortality. This suggests that a patient's current physical state which, is determined by their underlying health and as well as the disease process, matters more than their pre-operative health condition alone. This notion was further supported in the exploratory analysis, as again only the ASA score was associated with mortality (see Manuscript #2). In contrast to research in other patient populations frailty and age were not associated with mortality in this study. While it is possible that this discrepancy may be related to the relatively small number of mortality outcomes observed in this study, it is clear that further examination of prognostic factors for mortality in this patient population is required.

This present research was the first to examine prognostic factors for discharge to institution in older adults undergoing non-elective abdominal surgery. Frailty, the ASA score, and open surgery for benign disease were associated with discharge to institution, suggesting that both the pre-existing and the current state are important in this outcome. Further research is needed confirm that these factors are associated with discharge to institution in this patient population.

Implications for future research

Presently there is a disconnect between research and population trends. With increasing age the likelihood of undergoing emergency surgery is increased however research in this area continues to be poor (6,80). High quality studies examining prognostic factors for morbidity, mortality and discharge to institution are still needed. In addition, there needs to be communication between researchers making risk prediction models and clinicians who will us them, as the previous risk prediction models have had poor uptake into clinical practice (18). Lastly, given that the majority of clinical decisions are influenced by the initial decision to operate (78) risk prediction models should be largely based on information available prior to surgery if they are to impact clinical practice.

Implications for policy makers

Given that the population will continue to age, and that the demand for surgery in this population is expected to increase by 50% per decade (7), it would seem prudent for policy makers to support prognostic research. Prognostic models will help not only to provide information to patients on foreseeable risks, but will also help with quality improvement as it is will be possible to compare patient outcomes between institutions (19). These quality improvements will then help improve the overall efficiency of the health care system and contribute to it's sustainability (2).

APPENDIX ONE: *MEDLINE Search Strategy, performed June 11, 2012*

1. Abdom* [tiab]
2. Gastrointest* [tiab]
3. Surgery [tiab]
4. Digestive System Surgical Procedures [MH] NOT Endoscopy
5. #1 AND #3
6. #2 AND #3
7. #4 OR #5 OR #6

8. Non-elective [tiab]
9. Urgent[tiab]
10. Emergen*[tiab]
11. Acute*[tiab]
12. #8 OR #9 OR #10 OR #11

13. Aged [MH]
14. Geriatric* [tiab]
15. Elder* [tiab]
16. Senior* [tiab]
17. 'Older' [tiab]
18. #13 OR #14 OR #15 OR #16 OR #17

19. Incidence [MH]
20. Mortality [MH]
21. Follow-up studies [MH]
22. Prognos* [tiab]
23. Predict* [tiab]
24. Course* [tiab]
25. Risk* [tiab]
26. Adverse* [tiab]
27. Complication* [tiab]
28. Outcome* [tiab]
29. #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
30. #7 AND #12 AND #18 AND #29

APPENDIX TWO: *EMBASE Search Strategy, performed June 11, 2012*

1. ‘Abdomen’/exp
2. Gastrointest* :ti:ab
3. Surgery :ti:ab
4. ‘Abdominal Surgery’/exp
5. #1 AND #3
6. #2 AND #3
7. #4 OR #5 OR #6

8. Non-elective :ti:ab
9. Urgent :ti:ab
10. Emergen* :ti:ab
11. Acute* :ti:ab
12. #8 OR #9 OR #10 OR #11

13. 'Aged'/exp
14. Geriatric* :ti:ab
15. Elder* :ti:ab
16. Senior* :ti:ab
17. 'Older' :ti:ab
18. #13 OR #14 OR #15 OR #16 OR #17

19. ‘Incidence’/exp
20. ‘Mortality’/exp
21. ‘Follow-up’/exp
22. Prognos* :ti:ab
23. Predict* :ti:ab
24. Course* :ti:ab
25. Risk* :ti:ab
26. Adverse* :ti:ab
27. Complication* :ti:ab
28. Outcome* :ti:ab
29. #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28
30. #7 AND #12 AND #18 AND #29

APPENDIX THREE: *Data Extraction Form*

Study ID	***Refworks ID***	
	Assessor	
	Author	
	Year	
	Journal	
	Location	
Contact Info		
	Author Name	
	Institution	
	E-mail	
	Phone	
Eligibility		
Age	Aged ≥ 65 years of age	Yes ☐ Excluded ☐
≥ 90%	Abdominal surgery	Yes ☐ Excluded ☐
≥ 75%	Emergency Surgery	Yes ☐ Excluded ☐
	Primary Outcome?	Mortality ☐ Morbidity ☐
	Multivariate Analysis for Prognostic Factors used?	Yes ☐ Excluded ☐
Methods:	Study Type	Cohort ☐ RCT ☐
		Retrospective ☐ Prospective ☐
	Prognostic Factors Used in Univariate Analysis PF= Patient Factor (i.e. Age, Sex, ASA Score, Comorbidities, etc.) DF= Disease Factor (i.e. APACHE-II score, POSSUM score, presence of peritonitis, tumour stage, etc.) OF= Peri-operative Factor (i.e. timing of symptoms to admission/ OR, Type of Surgery, Surgeon's level of training, complications, blood transfusion, etc.)	
	Associations of Prognostic Factor with Outcome on Multi-variate Analysis	
	Accuracy of Prognostic Factor with Outcome	

Risk of Bias	**Please complete QUIPS tool for study**	
	Study Participation	High ☐ Moderate ☐ Low ☐
	Study Attrition	High ☐ Moderate ☐ Low ☐
	Prognostic Factor Measurement	High ☐ Moderate ☐ Low ☐
	Outcome Measurement	High ☐ Moderate ☐ Low ☐
	Study Confounding	High ☐ Moderate ☐ Low ☐
	Statistical Analysis and Presentation	High ☐ Moderate ☐ Low ☐
Participants	Number of participants	
	Age cut-off for inclusion	
	Average age	
	% male	
	Average BMI	
	Average LOS	
	% open surgery	
	% non-elective surgery	
	Mean Charlson Score	
	% HTN	
	% IHD (or CAD)	
	% DM	
	% CRF	
	% COPD	
	% CVD	
Primary Outcomes	**Please list for all factors associated in multivariate analysis**	
	In-hospital mortality (association)	
	30-day mortality (association)	
	Any complication (association)	
	Major complication (association)	
	Minor complication (association)	
Secondary Outcomes		

	LOS (association)	
	Discharge to institution (association)	
Additional Info		
	Source of Funding	
	Key Findings	
	Need to contact authors?	Yes☐ No ☐
	Additional References Identified	

APPENDIX FOUR: *The Comprehensive Geriatrics Assesment Form*

Capital Health

Comprehensive Geriatric Assessment Form

WNL = Within Normal Limits   ASST = Assisted
IND = Independent   DEP = Dependant

Patient contact (Pt.):
☐ Inpatient
☐ Clinic
☐ GDH
☐ NH
☐ Outreach
☐ Home
☐ Assisted living
☐ ER
☐ Other

How many month since well?

○ **Cognitive Status** ☐ WNL ☐ CIND/MCI ☐ Dementia ☐ Delirium MMSE ______ FAST ______
Chief lifelong occupation: ______ Education: (years) ______

○ **Emotional** ☐ WNL ☐ ↓ Mood ☐ Depression ☐ Anxiety ☐ Fatigue ☐ Other

○ **Motivation** ☐ High ☐ Usual ☐ Low **Health Attitude** ☐ Excellent ☐ Good ☐ Fair ☐ Poor ☐ Couldn't say

○ **Communication** **Speech** ☐ WNL ☐ Impaired **Hearing** ☐ WNL ☐ Impaired **Vision** ☐ WNL ☐ Impaired

○ **Strength** ☐ WNL ☐ Weak Upper: PROXIMAL DISTAL Lower: PROXIMAL DISTAL

		BASELINE (two weeks ago)	CURRENT (today)	NOTES
○ **Mobility**	Transfers	IND ASST DEP	IND ASST DEP	
	Walking	IND SLOW ASST DEP	IND SLOW ASST DEP	
	Aid	______	______	
○ **Balance**	Balance	WNL Impaired	WNL Impaired	
	Falls	N Y Number______	N Y Number______	
○ **Elimination**	Bowel	CONT CONSTIP INCONT	CONSTIP CONT INCONT	
	Bladder	CONT CATHETER INCONT	CATHETER CONT INCONT	
○ **Nutrition**	Weight	GOOD UNDER OVER OBESE	STABLE LOSS GAIN	
	Appetite	WNL FAIR POOR	WNL FAIR POOR	
○ **ADLs**	Feeding	IND ASST DEP	IND ASST DEP	
	Bathing	IND ASST DEP	IND ASST DEP	
	Dressing	IND ASST DEP	IND ASST DEP	
	Toileting	IND ASST DEP	IND ASST DEP	
○ **IADLs**	Cooking	IND ASST DEP	IND ASST DEP	
	Cleaning	IND ASST DEP	IND ASST DEP	
	Shopping	IND ASST DEP	IND ASST DEP	
	Medications	IND ASST DEP	IND ASST DEP	
	Driving	IND ASST DEP	IND ASST DEP	
	Banking	IND ASST DEP	IND ASST DEP	

Current Frailty Score:

Scale	Pt.	CG
1. Very fit		
2. Well		
3. Well c̄ Rx'd co-morbid disease		
4. Apparently vulnerable		
5. Mildly frail		
6. Moderately frail		
7. Severely frail		
8. Very severely ill		
9. Terminally ill		

○ **Sleep** ☐ Normal ☐ Disrupted ☐ Daytime drowsiness **Socially Engaged** ☐ Freq ☐ Occ ☐ Not

○ **Social** ☐ Married ☐ Divorced ☐ Widowed ☐ Single
Lives ☐ Alone ☐ Spouse ☐ Other
Home ☐ House (Levels __) ☐ Steps (Number__) ☐ Apartment ☐ Assisted living ☐ Nursing home ☐ Other
Supports ☐ Informal ☐ HCNS ☐ Other ☐ Req. more support ☐ None
Caregiver relationship ☐ Spouse ☐ Sibling ☐ Offspring ☐ Other
Caregiver Stress ☐ None ☐ Low ☐ Moderate ☐ High
Caregiver occupation: (CG)

☐ Advance directive in place?

○ **Code Status** ☐ Do not resuscitate ☐ Resuscitate ______

ACTION REQUIRED (check appropriate circles)

Problems:	Med adjust req.	Associated Medication: (*mark meds started in hospital with an asterisks)
1. RFR	○	
2.	○	
3.	○	
4.	○	
5.	○	
6.	○	
7.	○	
8.	○	
9.	○	
10.	○	
11.	○	

Assessor/Physician: ______ Date: ______ YYYY/MM/DD

Assessment Forms
CD0184MR_06_09

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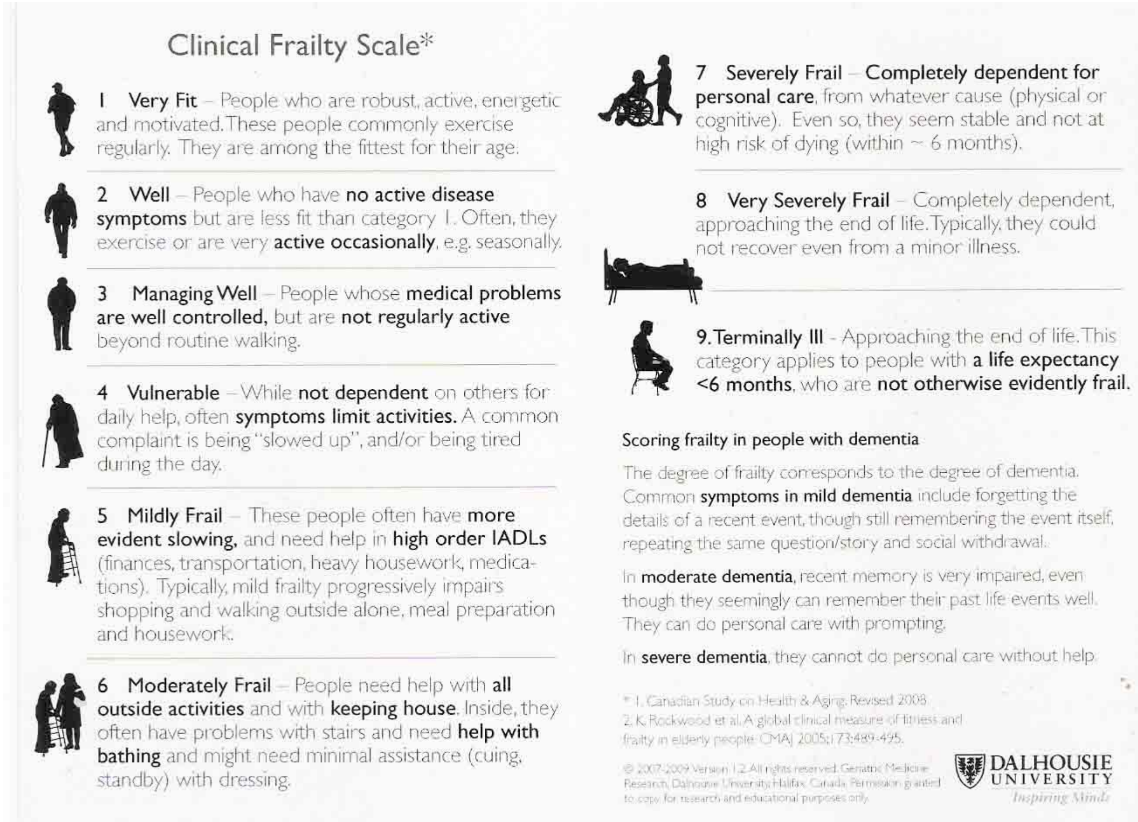
APPENDIX FIVE: *Factors included in the Frailty Index* [62].

Deficit Count	List of Variables Included in the FI-CGA	Cut Point
1.	Help bathing	Yes=1, No=0
2.	Help dressing	Yes=1, No=0
3.	Help getting in/out of chair	Yes=1, No=0
4.	Help walking around house	Yes=1, No=0
5.	Help with mobility outside house	Yes=1, No=0
6.	Help eating	Yes=1, No=0
7.	Help grooming	Yes=1, No=0
8.	Help using toilet	Yes=1, No=0
9.	Help up/down stairs	Yes=1, No=0
10.	Help lifting 10 lbs	Yes=1, No=0
11.	Help shopping	Yes=1, No=0
12.	Help with housework	Yes=1, No=0
13.	Help with meal preparations	Yes=1, No=0
14.	Help taking medication	Yes=1, No=0
15.	Help with finances	Yes=1, No=0
16.	Urinary incontinence	Yes=1, No=0, catheter=1
17.	Bowel incontinence	Yes=1, No=0
18.	Lost more than 10 lbs in last year	Yes=1, No=0
19.	Self-rating of health	Poor=1, Fair=0.75, Good=0.25, Very Good to Excellent=0
20.	History of falls	Yes=1, No=0
21.	Impaired vision	Yes=1, No=0
22.	Impaired hearing	Yes=1, No=0
23.	Difficulty speaking	Yes=1, No=0
24.	Sleep disturbance	Yes=1, No=0
25.	High blood pressure	Yes=1, Suspect=0.5, No=0
26.	Heart rhythm disorder	Yes=1, Suspect=0.5, No=0
27.	Heart attack	Yes=1, Suspect=0.5, No=0
28.	Congestive heart failure	Yes=1, Suspect=0.5, No=0
29.	Peripheral vascular disease	Yes=1, Suspect=0.5, No=0
30.	Stroke	Yes=1, Suspect=0.5, No=0
31.	Cancer	Yes=1, Suspect=0.5, No=0
32.	Diabetes mellitus	Yes=1, Suspect=0.5, No=0
33.	Arthritis	Yes=1, Suspect=0.5, No=0
34.	Chronic lung disease	Yes=1, Suspect=0.5, No=0
35.	Kidney disease	Yes=1, Suspect=0.5, No=0
36.	Constipation	Yes=1, No=0
37.	Other medical problems	None=0; Maximum=2
38.	Depression	Yes=1, Suspect=0.5, No=0
39.	Anxiety	Yes=1, Suspect=0.5, No=0
40.	Alcohol use	Yes=1, Suspect=0.5, No=0
41.	Other psychiatric illness	Yes=1, Suspect=0.5, No=0
42.	Timed Up and Go	>14=1, 10–14=0.5, <10=0
43.	Functional Reach	≤15=1, 15–25=0.5, ≥25=0
44.	Mini-Mental State Examination	<10=1, 11–17=0.75, 18–20=0.5, 20–24=0.25, >24=0
45.	Measured systolic hypertension	>160=1, >141–160=0.5
46.	Measured diastolic hypertension	>100=1, >90–100=0.5
47.	Measured orthostatic hypotension	>20=1, 14–19=0.5
48–52.	Medications	>5 medications=1, >10=2, >15=3, >20=4,

APPENDIX SIX: *The CSHA Clinical Frailty Scale* [63].


Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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APPENDIX SEVEN: *Pierre-Clavien Classification* [27].

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III	Requiring surgical, endoscopic or radiological intervention.
Grade IIIa	Intervention not under general anesthesia.
Grade IIIb	Intervention under general anesthesia.
Grade IV	Life-threatening complication (Including CNS complications)* requiring IC/ICU management.
Grade IVa	Single organ dysfunction (Including dialysis).
Grade IVb	Multiorgan dysfunction.
Grade V	Death of a patient.
Suffix "d"	If the patient suffers from a complication at the time of discharge (see examples in Table-2), the suffix "d" (for "disability") is added to the respective grade of complication. This label indicates the need for a follow-up to fully evaluate the complication.

**Brain hemorrhage, ischemic stroke, subarrachnoidal bleeding, but excluding transient ischemic attacks. CNS = central nervous system; IC = intermediate care; ICU = intensive care unit. Source = Dindo D, Demartines N, Clavien PA = Classification of surgical complications = a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004; 240: 205-13.*

APPENDIX EIGHT: *Copyright Release for Manuscript One*.

[June 13, 2013]

Canadian Journal of Surgery
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