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Functional Status is Key to Long-Term Survival In Emergency General Surgery Conditions

Vanessa P. Ho, MD, MPH[1,2], Wyatt P. Bensken, PhD[2], J. Alford Flippin, MD[1], Heena P. Santry, MD, MPH[3], Jeffrey A. Claridge, MD, MS[1], Christopher W. Towe, MD[4], Siran M. Koroukian, PhD[2]

[1]Department of Surgery, MetroHealth Medical Center and Case Western Reserve University School of Medicine, Cleveland Ohio

[2]Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland Ohio

[3]Department of Surgery, Kettering Hospital, Columbus Ohio

[4]Department of Surgery, University Hospitals Cleveland Medical Center and Case Western Reserve University School of Medicine, Cleveland Ohio

Abstract

Background: Emergency General Surgery (EGS) conditions in older patients constitutes a substantial public health burden due to high morbidity and mortality. We sought to utilize a supervised machine learning method to determine combinations of factors with the greatest influence on long-term survival in older EGS patients.

Methods: We identified community dwelling participants admitted for EGS conditions from the Medicare Current Beneficiary Survey linked with claims (1992–2013). We categorized 3 binary domains of multimorbidity: chronic conditions, functional limitations, and geriatric syndromes

Corresponding Author: Vanessa P. Ho, MD, MPH, Department of Surgery and Population and Quantitative Health Sciences, Division of Trauma, Critical Care, Burn, and Acute Care Surgery, 2500 MetroHealth Drive, Cleveland, OH 44109, vho@metrohealth.org, Phone: 216-778-4979, Fax: 216-778-1351.

Author Contributions:

Author	Literature Review	Study Design	Data Collection	Analysis and Interpretation	Manuscript Writing	Critical Revisions
VPH	X	X	X	X	X	X
WPB	X	X	X	X	X	X
JAF	X				X	X
HPS	X	X		X	X	X
JAC	x	X		X	X	X
CWT	X			X	X	X
SMK	X	X	X	X	X	X

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(such as vision/hearing impairment, falls, incontinence). We also collected EGS disease type, age, and sex. We created a classification and regression tree (CART) model to identify groups of variables associated with our outcome of interest, 3-year survival. We then performed Cox proportional hazards analysis to determine hazard ratios for each group, with the lowest risk group as reference.

Results: We identified 1,960 patients (median age 79 [IQR: 73, 85], 59.5% female). The CART model identified the presence of functional limitations as the primary splitting variable. The lowest risk group were patient aged ≤81 with biliopancreatic disease and without functional limitations. The highest risk group was men aged ≥75 with functional limitations (HR 11.09 (95% CI 5.91–20.83). Notably absent from the CART model were chronic conditions and geriatric syndromes.

Conclusions: More than the presence of chronic conditions or geriatric syndromes, functional limitations are an important predictor of long-term survival and must be included in pre-surgical assessment.

Keywords

Emergency General Surgery; Geriatric Surgery; Multimorbidity; Frailty; Functional Status

Introduction

Patients who have Emergency General Surgery (EGS) diagnoses, such as cholecystitis and perforated ulcers, account for nearly 3 million admissions a year, of whom approximately 30% undergo surgical therapy.(1) Admissions for EGS diagnoses are expensive; annual estimated costs are expected to be $41 billion by 2060.(2) Nearly one-third of EGS disease occurs in older adults, many of whom present for surgery with pre-existing complex medical disease and frailty.(3–6) For Medicare patients, EGS can be a catastrophic, life-changing, unexpected event, with both high morbidity and high mortality. In-hospital mortality is estimated to range from 5–15%, and mortality and morbidity continues to climb after discharge.(7–10) In one study of Medicare patients over 65, one quarter of hospital survivors were deceased or had experienced a significant loss of independence requiring change in residence to a facility in nine months following discharge.(11)

For elective surgical patients, it is well known that baseline frailty and functional status is an important predictor of postoperative outcomes, leading to programs that encourage preoperative conditioning, sometimes referred to as “prehabilitation.”(12, 13) Unfortunately, due to the inherently emergent nature of the diseases, patients with EGS conditions not only have higher risk for the same procedure performed electively (14) but also have no opportunity to mitigate preexisting risk factors. While prospective frailty measurement in older EGS patients has been described,(15) it can be logistically difficult to obtain high quality baseline frailty information on EGS patients due to the emergent nature of these diseases. Another method to measure frailty status has been through the use of administrative data to generate summary frailty score,(16–18) but these measures do not allow clinicians to identify specific risk factors and can be difficult to apply in a clinical setting due to a large number of factors required for calculation. Identification of patients at high risk of long-term mortality would allow surgeons to counsel patients and may also allow identification of postoperative intervention targets to help patients obtain a favorable recovery trajectory.

Another method of measuring patient health status may be through a framework called Complex Multimorbidity, which allows phenotypic description of patient vulnerability based on whether any of three key domains are present: chronic conditions, functional limitations, or geriatric syndromes.(19) An advantage of this system is that this score, which ranges from MM0 (no domains present) to MM3 (all three domains present), is derived from survey data and the domains and their components can be evaluated for contribution to outcomes. Our group has previously published data regarding the application of this framework in the EGS population, demonstrating that the summary multimorbidity score can efficiently risk stratify groups for long-term survival.(20) The purpose of our current study was to use classification and regression tree analysis, a supervised machine learning method, to determine if specific combinations of baseline patient factors could be used to assess risk of long-term mortality after admission for emergency general surgery diseases.

Methods

Data Source

We utilized data from the Medicare Current Beneficiary Survey (MCBS), a nationally representative, continuous longitudinal panel of Medicare beneficiaries surveyed that has been carried out continuously for over twenty years.(21, 22) Each participant is surveyed 12 times over four years in multiple domains including health, functional status, and healthcare utilization. Survey items on functional status include activities of daily living (ADLs such as walking, bathing, using the toilet), instrumental ADLs (iADLs such as housework, shopping, using the telephone), and other health related items (such as need for assistance, and cognitive ability). In this study we specifically utilized MCBS data on community-dwelling participants from 1992 – 2013. Due to a major data format change in the MCBS, data for 2014 were not released and we elected to perform the analysis on the historical dataset which allowed 22 years of continuously collected data.(21) Only complete cases including patients receiving care through the traditional fee for service system were included.

Inclusion Criteria

The inclusion criteria in this population have been previously described in greater detail.(23) Briefly, we identified community-dwelling patients who had a hospitalization related to an EGS condition using Medicare diagnoses and procedure codes, defined as the index EGS admission. We restricted to those over 65 years old, who had received their care through the fee-for-service system, who were verified to be community-dwelling at the time of the index admission, and had valid baseline survey data completed prior to the index admission (Figure 1). EGS disease and procedure codes were derived from a method published by Smith et al.(11) EGS conditions were categorized into the following categories: biliopancreatic (such as cholelithiaisis, choledocholithiasis, and pancreatitis), colon (such as perforation, diverticulitis and other infectious colitis, acute complications of colon neoplasms), peptic ulcer/gastrointestinal bleed (such as gastroduodenal ulcers, upper and lower bleeding), and small bowel/appendix/other (such as bowel obstruction, acute mesenteric ischemia, appendicitis, peritonitis, solid organ rupture and hemoperitoneum).

Outcome of Interest

Our outcome of interest was 3-year survival from date of admission for the EGS condition. Using the MCBS data, we were able to identify if an individual died and their date of death, and for those who did not die we identified their last year of enrollment in MCBS and set December 31 of that year to be their censoring date. As the MCBS is a 4-year panel survey, we limited our follow-up time to a maximum of 3 years.

Independent Variables

The independent variables included in this study were: if someone underwent an operative procedure for their EGS disease, age at admission for the EGS condition, sex (male/female), and EGS condition category. Additionally, we used a Complex Multimorbidity framework which identifies three key domains: functional limitations, geriatric syndromes, and chronic conditions. The components of this framework in this study population have been previously described,(19, 23) and are detailed in Table 1. We included each of these domains independently, as well as the composite sum of these domains (MM0 – MM3) in the analysis.

Statistical Analysis

In this study we combined traditional statistical approaches with supervised machine learning. We compared functional limitations (FL), geriatric syndromes (GS), and chronic conditions (CC) between those who died and were alive/censored using Chi-squared analyses, with Bonferroni correction. While our initial alpha was 0.05, the adjusted alpha, after accounting for multiple comparisons, was 0.017.

Then, we used classification and regression tree analysis (CART) – a supervised machine learning technique which recursively partitions the data, by testing each variable and selects one that best reduces the Gini index, a measure of inequality among values in a frequency distribution.(24) Ultimately, this creates groups that are more homogenous and identifies factors that best separate the population, in this case with respect to survival, given our independent predictors. There are a number of parameters that CART utilizes to construct the tree. Our goals in constructing this CART was to create a reasonably simple model without overfitting.

We set our parameters to allow a maximum depth of 3, so that no more than three variables would influence the membership in the terminal node groups, allowing for model simplicity. Recognizing that a small subgroup of patients which would be not representative could influence terminal nodes, we limited our final terminal node size to a minimum of 20. We also set our minimum complexity parameter (Gini index) of 0.001, to allow a variable to be included by just improving the model slightly. We used 20-fold cross validation in model building. The model was also pruned to prevent overfitting. Once we identified the distinct subgroups, we used Cox proportional hazards models to establish hazard ratios, with 95% confidence intervals for each of these groups, with the reference group being those with the best survival. In our main CART analysis, we utilized the independent variables as listed above. We then performed a second CART analysis, using the components of the most influential Complex Multimorbidity domain to determine if there were specific components that were strongly associated with mortality, using the same parameters as described above.

We used SAS Version 9.4 for data cleaning and R version 3.4.1, including 'rpart' and 'partykit', packages for the CART analysis. Use of these data and this project were approved by the Case Western Reserve University Institutional Review Board.

Results

We identified a cohort of 1,960 patients who met inclusion criteria for this analysis (Figure 1). The median age was 79 [IQR 73,84], and 1,166 (60%) were female. Of these patients, 1,243 (63%) were nonoperatively managed. Detailed descriptions of multimorbidity and functional impairments in this population have been previously described.(23) The median follow-up period for the cohort was 377 days [IQR 138,621].(20) There were 376 individuals who died (19.2%), which occurred at a median time of 87 days [IQR 32, 300].(20)

There were significant differences in functional limitations and chronic conditions between those were alive/censored and those who died, although these differences were not seen for geriatric syndromes (Table 1). The most common functional limitation, regardless of survival, was difficulty stooping/crouching/kneeling with 80.6% of those where alive/censored and 85.6% of those who died reporting this limitation. There was a substantially higher prevalence of nearly all functional limitations among those who died. The most common chronic condition was non-rheumatoid arthritis, with a higher prevalence among those who were alive/censored (69.6%) compared to those who died (62.8%) (Table 1). Difficulty lifting or carrying ten pounds was present in 50.4% of survivors and in 70.7% of those who died. While those who died commonly had a higher prevalence of chronic conditions, this difference was not as clear as functional limitations. Finally, the most common geriatric syndrome was hearing impairment with a prevalence of 46.8% and 52.1% among those who were alive/censored and those who died, respectively.

Our main CART model, shown in Figure 2, identified 8 subgroups. Hazard ratios corresponding to all identified subgroups are listed in Table 2, with the lowest risk group serving as the reference for the remainder of the groups. The first node in the model is the presence of functional limitations. Other nodes which are present in the model are age and sex. Absent from the model whether a surgical operation was performed, the presence of chronic conditions, or geriatric syndromes. Interestingly, the EGS disease type was only a factor for the arm of the model that included patients without functional limitations and who were under 82 years old. Biliopancreatic disease in this population had the highest survival. Patients who had functional limitations at baseline had higher mortality, with the lowest survival rates in men aged 75 years and older (HR 11.09, 95% CI 5.91, 20.83). The age breakpoint for survival groups among men and women with functional limitations differed; for women the age breakpoint was 89 years, whereas for men the age breakpoint was 14 years younger, at 75 years. The interaction of age and sex appears important in every group except those who are functionally independent and younger than age 82.

The second CART model was developed, shown in Figure 3, using the same statistical parameters and including the component factors for "functional limitations" as candidate variables, to determine if specific functional impairments were particularly strong influences on long-term mortality. For this model, a patient stating that they had difficulty lifting or carrying 10 pounds became the first node of the model. This model was otherwise relatively similar to the main CART model, whereby younger patients without this functional limitation and with biliopancreatic disease had the best survival. Again, older male patients with strength limitation had the poorest long-term survival. Corresponding hazard ratios are listed in Table 3.

Discussion

Older patients who are admitted with emergency general surgery conditions are an extremely high-risk population, with 19% of this patient population with known mortality in our study period, with an average follow-up time of roughly one year. The presence of functional limitations was identified by the CART model as the first point to discriminate groups with higher and lower survival. Other important factors in the model included age and sex, with females having generally higher survival rates than males. Notably absent from the model was the use of operative management for the EGS disease, the presence of chronic conditions, or the presence of geriatric syndromes. Further examination identified "difficulty lifting" as a key functional status variable. While there are limitations with our data, we believe that the identification of functional limitations as a key prognostic factor for long-term survival deserves further and future exploration.

Achieving shared decision making and informed consent in EGS diseases requires discussion of likely outcomes. Accurate assessment of risk and recovery may prevent patients from undergoing procedures with a high chance of futility or, conversely, support the decisions of relatively healthy older patients to pursue aggressive life-prolonging care. It has been demonstrated that surgeon perception of risks for emergency general surgery procedures can vary substantially, and that the use of surgical risk calculators decreases such variation. Surgical risk calculators have been developed as tools to predict outcomes, including the American College of Surgeons NSQIP risk calculator and the Emergency Surgery Score (and subsequently developed POTTER calculator).(25–30) These risk tools, developed using data provided by NSQIP, have two major limitations: they do not include any prognostication for patients who undergo nonoperative management, and they do not examine outcomes beyond thirty days. These gaps are quite meaningful in the prognostication of EGS conditions. Approximately 70% of patients of all ages who are admitted for EGS diseases are nonoperatively managed,(3) and the outcomes of these patients have not been well documented. Also, a large proportion of mortality in the EGS patient population occurs after 30 days; in our study, only approximately one-quarter of deaths occurred within the first 30 days.

The impact of baseline health status such as frailty, multiple chronic conditions, or multimorbidity on outcomes after EGS admission is increasingly being acknowledged,(16, 18, 31–36) although many knowledge gaps remain in this area, particularly in long-term outcomes. Interestingly, the presence of chronic conditions, which varied between survivors and nonsurvivors, did not strongly differentiate enough between outcome groups to be included in the final CART models. Chronic conditions are the most easily tracked factor in the medical record and in administrative data as these correspond directly to diseases with ICD-10 codes, and the presence of comorbidities tend to be the driving factor behind many frailty measurement methods. Frailty has been associated with increased postoperative complications, length of stay, and adverse discharge disposition (to skilled nursing facility or in-hospital mortality).(15–17, 32) The most commonly used frailty measures are derived from NSQIP and are influenced mainly by the presence of chronic conditions. A Modified Frailty Index (mFI-5) for use with NSQIP data has five factors weighted equally: functional dependence, diabetes, COPD, congestive heart failure, and hypertension requiring medications.(37) Though the mFI-5 has been shown to be predictive of 30-day mortality and postoperative complications, the impact of functional limitations may be underappreciated given the equal weighting of factors. Another commonly used measure is the Clinical Frailty Scale, a Likert-type point scale representing an overall score ranging from very fit to terminally ill.(38) The Clinical Frailty Scale is easy to measure in the clinical setting, but may not be as useful for the development of future interventions. Our scale differs as we can tease out the key domains and specific risk factors, and hopefully use these as targets for future intervention.

We have demonstrated that the assessment of pre-intervention functional status may allow for a simple and tailored assessment of a patient's postoperative survival trajectory after EGS. While the focus on functional status as a key mediator of outcomes for surgical diseases outcomes is not new, it has not been extensively studied in EGS patients. Functional status is one of the key screening questions in the American College of Surgeons Strong for Surgery program, which is designed to optimize patients for elective surgery.(12) Strong for Surgery recommends "prehabilitation", preoperative optimization of modifiable risk factors, for patients with functional limitations or frailty who are planning to undergo elective surgery. Unfortunately, EGS patients do not have prior knowledge of their surgical disease and therefore no opportunity to engage in "prehabilitation". However, most patients do survive past 30 days, with or without surgery and there is often a long period of time in which some patients have a health decline. This protracted course of recovery may afford the patient's clinician team an opportunity for post-admission interventions, whether these are conditioning programs to improve the patient's quality of life or directed and deliberate discussions about long-term goals of care with the patients and their families. Our analysis identified "difficulty lifting" as a functional task which discriminated groups in our dataset, but this finding requires further study. The significance of this finding is yet unknown—however, it is likely that this is a surrogate marker for frailty rather than pointing to a specific key exercise which can change long-term outcomes. More high-quality data and prospective data on EGS patients and their long-term functional status is needed to further improve meaningful prognostication and develop interventions to change outcomes in this patient population.

Our study has several important limitations. Given that our hospitalization data was identified via Medicare billing codes, our knowledge of the clinical factors pertaining to the EGS admission episode are not available through the data in this administrative dataset. For example, we had no specific data from the hospitalization for EGS disease on such measures as severity of disease, reasons behind treatment decisions or decisions to pursue operative management, patient preferences, or other factors that would affect treatment. We also rely upon patient reported survey factors for the patient's baseline medical history and disease profiles. While patient self-report has been validated in the past for being valuable for outcome prognostication, these measures are theoretically limited by a patient's understanding of their medical diseases and diagnoses. In addition, despite the large dataset of EGS patients, this encompasses a variety of disease subtypes and a wide variety of patient multimorbidity phenotypes. Unfortunately, these patient subgroups are too small for in-depth analysis. With regard to patient sex, it appears that sex is an important factor in long-term survival; here we equate biological sex with reported sex, but we cannot be sure that this is the case. Lastly, we note that these data are also older, prior to the wide use of laparoscopy, for example. However, due to data structure changes, we are unable to utilize more recent continuous data. We believe our data, although historical, are still relevant today as our mortality rates are similar to other studies on EGS and outcomes (from more recent studies?).(7, 11, 18) Survival was measured up to 3 years, but many patients were censored prior to this time and we may have underestimated mortality in the patient population. Despite these limitations, the CART analysis provided meaningful risk groups for the older population of EGS patients.

Conclusions

For older adults who are admitted with emergency general surgery conditions, subsequent mortality is high. The presence of functional limitations is an extremely important indicator of long-term risk in this patient population and must become a standard part of the patient evaluation and surgical history. Better understanding of the chronic and acute risks to the patient will help surgeons and patients participate in shared decision making to ensure alignment of goals and treatment plans.

Author Disclosures:

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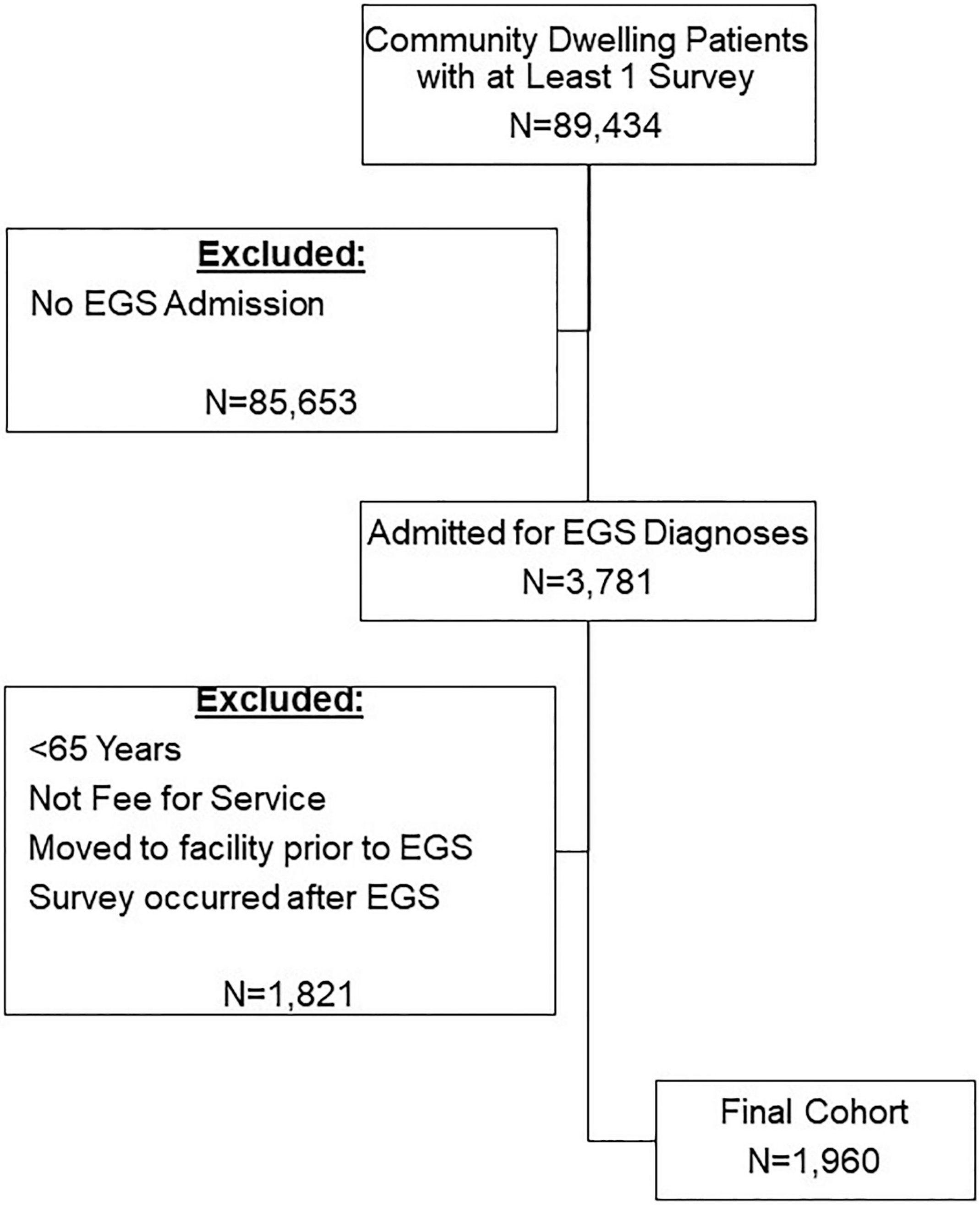

Figure 1:
Patient Inclusion

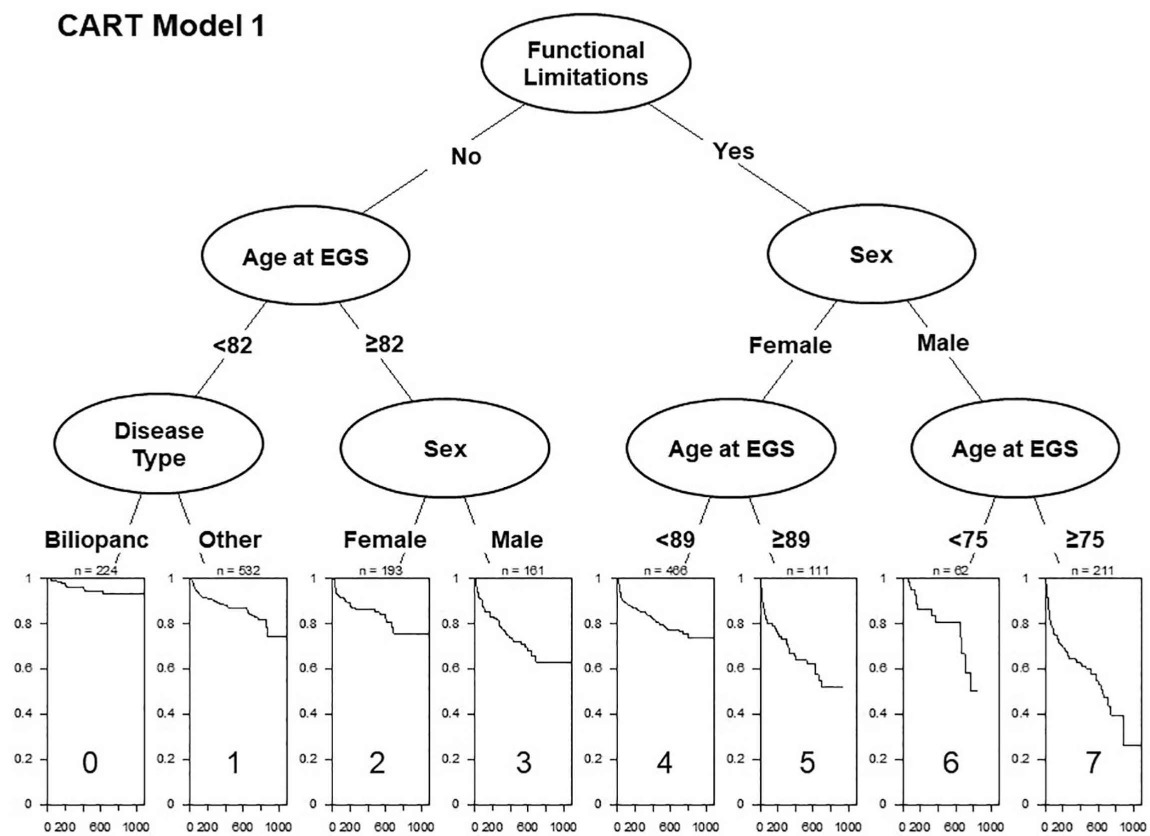

Figure 2: CART Model 1

CART (Classification and Regression Tree) Model; inputs included multimorbidity key domains, age at index admission, sex, summary multimorbidity score (0–3), and EGS condition category. This CART shows 8 subgroups of patients, with group 0 being reference for Hazard Ratios found in Table 2.

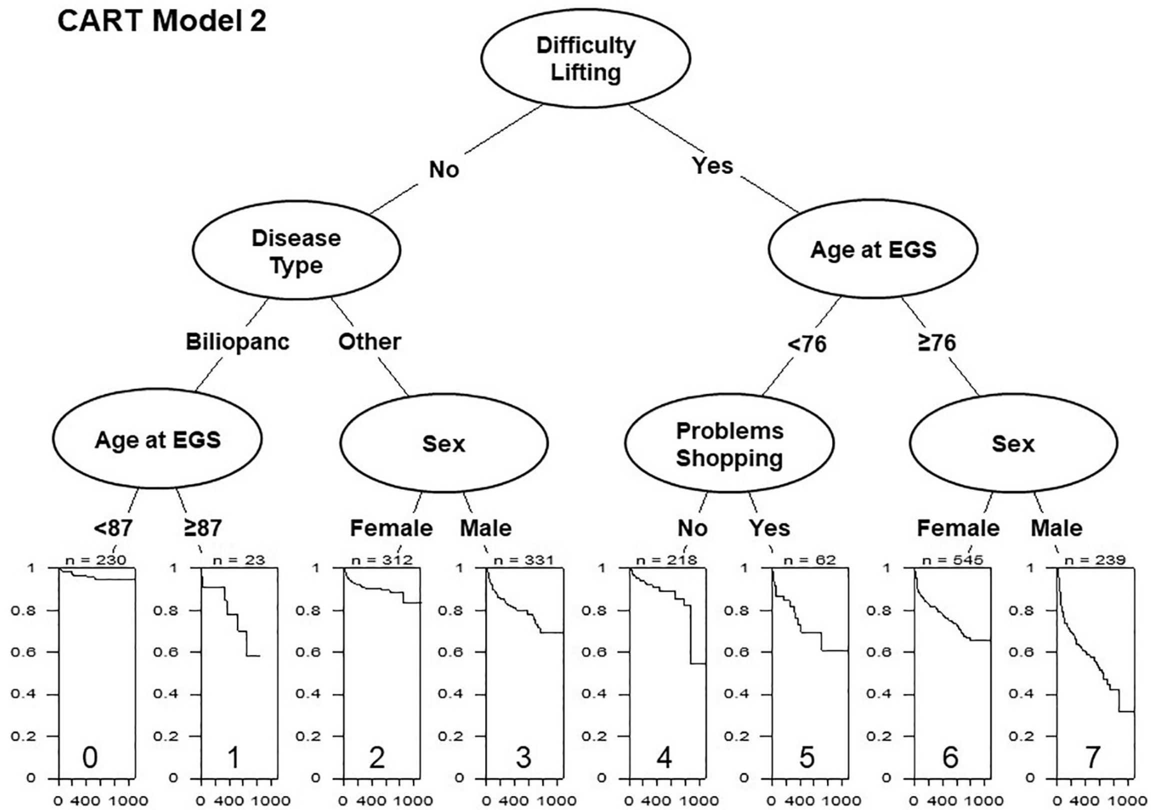

Figure 3: CART Model 2

CART (Classification and Regression Tree) Model; inputs included component factors of functional limitations, key domains of chronic conditions and geriatric syndromes, age at index admission, sex, summary multimorbidity score (0–3), and EGS condition category. This CART shows 8 subgroups of patients, with group 0 being reference for Hazard Ratios found in Table 3.

Table 1:

Patient Cohort, by Survival

Complex Multimorbidity Domains	Alive/Censored N=1,584	Deceased N=376	p-value
Functional Limitations	**628 (39.6)**	**222 (59.0)**	**< 0.001**
Difficulty stooping/crouching/kneeling	1277 (80.6)	322 (85.6)	
Difficulty walking 2–3 blocks	966 (61.0)	291 (77.4)	
Difficulty lifting/carrying 10 pounds	798 (50.4)	266 (70.7)	
Difficulty extending arms above shoulder	567 (35.8)	174 (46.3)	
Difficulty writing/handling object	531 (33.5)	182 (48.4)	
Any difficulty walking	501 (31.6)	188 (50.0)	
Any difficulty doing heavy housework	416 (26.3)	115 (30.6)	
Any difficulty getting in/out of bed/chair	300 (18.9)	112 (29.8)	
Any difficulty bathing/showering	277 (17.5)	120 (31.9)	
Any difficulty shopping	210 (13.3)	83 (22.1)	
Any difficulty dressing	177 (11.2)	80 (21.3)	
Any difficulty doing light housework	164 (10.4)	74 (19.7)	
Any difficulty preparing meals	152 (9.6)	70 (18.6)	
Any difficulty using toilet	126 (8.0)	61 (16.2)	
Any difficulty using telephone	122 (7.7)	58 (15.4)	
Any difficulty with managing money	93 (5.9)	41 (10.9)	
Any difficulty eating	49 (3.1)	32 (8.5)	
Chronic Conditions	**1,228 (77.5)**	**322 (85.6)**	**0.001**
Non-rheumatoid arthritis	1103 (69.6)	236 (62.8)	
Hypertension/High Blood Pressure	1065 (67.2)	247 (65.7)	
Other heart condition	499 (31.5)	121 (32.2)	
Any cancer (excld. Skin)	386 (24.4)	105 (27.9)	
Myocardial Infarction/heart attack	311 (19.6)	93 (24.7)	
Emphysema/asthma/COPD	296 (18.7)	86 (22.9)	
Rheumatoid arthritis	250 (15.8)	63 (16.8)	
Stroke/brain hemorrhage	245 (15.5)	88 (23.4)	
Heart rhythm problems	169 (10.7)	33 (8.8)	
Heart value issues	82 (5.2)	17 (4.5)	
Congestive heart failure	62 (3.9)	13 (3.5)	
Diabetes	11 (0.7)	< 11 *	
Geriatric Syndromes	**1,494 (94.3)**	**357 (94.9)**	**0.724**
Hearing problems	741 (46.8)	196 (52.1)	
Vision problems	637 (40.2)	181 (48.1)	
Urine problems	443 (28.0)	140 (37.2)	
Time feeling sad or blue	214 (13.5)	46 (12.2)	

Complex Multimorbidity Domains	Alive/Censored N=1,584	Deceased N=376	p-value
Trouble Eating Solid Foods	207 (13.1)	81 (21.5)	
Trouble concentrating	170 (10.7)	60 (16.0)	
Memory loss	155 (9.8)	53 (14.1)	
Problems making decisions	100 (6.3)	42 (11.2)	

*Other demographics previously reported (Ho, et al. JAMA Surgery). Groups smaller than 11 individuals are not reported

Table 2.

CART Model 1 Hazard Ratios

Group	Factors	HR (95% CI)
0	Functional Limitations = No Age at EGS < 82 Disease Type = Biliopancreatic	*Ref*
1	Functional Limitations = No Age at EGS < 82 Disease Type = Not Biliopancreatic	2.79 (1.48, 5.27)
2	Functional Limitations = No Age at EGS ≥ 82 Sex = Female	3.59 (1.80, 7.17)
3	Functional Limitations = No Age at EGS ≥ 82 Sex = Male	6.36 (3.29, 12.32)
4	Functional Limitations = Yes Sex = Female Age at EGS < 89	4.30 (2.30, 8.06)
5	Functional Limitations = Yes Sex = Female Age at EGS ≥ 89	8.96 (4.60, 17.47)
6	Functional Limitations = Yes Sex = Male Age at EGS < 75	4.95 (2.22, 11.05)
7	Functional Limitations = Yes Sex = Male Age at EGS ≥ 75	11.09 (5.91, 20.83)

Table 3.

CART Model 2 Hazard Ratios

Group	Factors	HR (95% CI)
0	Difficult Lifting = No Disease Type = Biliopancreatic Age at EGS < 87	*Ref*
1	Difficult Lifting = No Disease Type = Biliopancreatic Age at EGS ≥ 87	7.30 (2.60, 20.52)
2	Difficult Lifting = No Disease Type = Not Biliopancreatic Sex = Female	2.56 (1.22, 5.40)
3	Difficult Lifting = No Disease Type = Not Biliopancreatic Sex = Male	5.67 (2.82, 11.38)
4	Difficult Lifting = Yes Age at EGS < 76 Problems Shopping= No	2.87 (1.32, 6.24)
5	Difficult Lifting = Yes Age at EGS < 76 Problems Shopping= Yes	7.85 (3.43, 17.94)
6	Difficult Lifting = Yes Age at EGS ≥ 76 Sex = Female	7.07 (3.60, 13.88)
7	Difficult Lifting = Yes Age at EGS ≥ 76 Sex = Male	14.12 (7.13, 27.97)