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High Risk Comorbidity Combinations in Older Patients undergoing Emergency General Surgery

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Abstract

Background/Objectives: Over a million older patients are admitted yearly for emergency general surgery (EGS) conditions in America, of which seven procedure types dominate (colon, small bowel, gallbladder, ulcer disease, adhesiolysis, appendix, and laparotomy operations). A higher comorbidity burden is known to increase mortality in this population, but the impact of specific comorbidity combinations is unknown. Our objectives are to: 1) Characterize the distribution of procedures, comorbidities, and outcomes for older patients undergoing EGS. 2) Apply a data-driven approach (Association Rule Mining) to identify comorbidity combinations associated with disproportionately high mortality.

Design, Setting, and Participants: Cross-sectional study of patients aged 65 and older who underwent one of the seven above procedures, taken from the 2011 Nationwide Inpatient Sample. 280,885 patient encounters were identified.

Measurements: In-hospital mortality, procedures, and comorbidities based on the Elixhauser comorbidity index.

Results: Overall mortality was 5.6%. The most common procedures were gallbladder (33.7%), ulcer surgery (21.5%), and adhesiolysis (21.0%). Mortality increased for all procedures as patients aged. Comorbidities associated with the highest mortality included coagulopathy (adjusted odds ratio [OR]: 3.74, 95% confidence interval [3.41 – 4.11], $p < .001$), fluid & electrolyte disorders (FED) (OR: 2.89 [3.66 – 3.14], $p < .001$), and liver disease (OR: 1.89 [1.61 – 2.22], $p < .001$). Three-way comorbidity combinations most highly associated with mortality were coagulopathy, FED,

and peripheral vascular disease (OR: 5.10 [4.17– 6.24], $p<.001$), and coagulopathy, FED, and chronic pulmonary disease (OR: 4.83 [4.00 – 5.82], $p<.001$).

Conclusions: For older patients, combinations of comorbidities portend additional risk beyond single comorbidities, and the associated risk burden is driven by the specific constellation of comorbidities present. Future work must continue to examine the effect of co-occurring diseases to provide personalized and realistic prognostication for older patients undergoing emergency general surgery.

Keywords

Older adult; Geriatrics; Surgery; Comorbidities; Multimorbidity

BACKGROUND

Emergency general surgery (EGS) conditions account for a substantial and increasing burden of disease within the United States, with nearly 3 million admissions per year.¹ Half of patients admitted for EGS are over the age of 60, and 28% of these patients require an unplanned surgery during the admission.¹ Amongst patients who undergo surgery, seven procedures account for the majority of the attributable burden of admissions, deaths, and costs, which include: colon operations, small bowel operations, gallbladder operations, surgical treatment of peptic ulcer disease, lysis of peritoneal adhesions, appendectomy, and other laparotomy.² Emergency surgery in the older patient is a high risk undertaking, as inpatient mortality increases with age, even when adjusted for comorbidities; nationwide mortality for EGS cases is 5.0% for patients aged 65–69 but increases steadily to 20.4% for patients aged 90 and older.³ Serious morbidity for this patient group is also high, with a reported range from 17–83%.^{6–9} Cost for these patients is estimated at \$28 billion per year, and are projected to increase to \$41 billion by 2060, with older patients accounting for a disproportionate share of the cost.⁴

Despite the widespread recognition that older patients have high mortality and morbidity after emergency surgery, little is known about how specific comorbidities or combinations of comorbidities affect mortality in the post-operative setting. Older patients with EGS conditions often present with a background that includes complex medical issues that may include comorbidities, disability, or frailty. The presence of multiple comorbid conditions presents challenges as the use of health care services and costs increase with each additional condition.⁵ Increases in comorbidity scores are also associated with increased risk of death and complications,⁶ but it is unknown which comorbidities or specific comorbidity combinations pose the greatest risk. For older individuals, we need to better understand the complex interaction between preexisting comorbidities and the outcomes experienced.

We hypothesize that it is not only the presence of multiple comorbid conditions but the specific constellation (or combination) of comorbid conditions that can adversely affect the risk of mortality from unplanned surgery on the older patient. The aim of this paper is to apply a data-driven approach to identify combinations of comorbidities that are associated with disproportionate in-hospital mortality.

METHODS

Study Data and Population

This is a cross-sectional study using secondary data from the 2011 Nationwide Inpatient Sample (NIS). The NIS is part of the Healthcare Cost and Utilization Project and is the largest all-payer inpatient database in the United States with a nationally representative sample of approximately 8 million inpatient discharges each year.⁷ Data elements include patient demographic variables, insurance status, International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes, hospital characteristics, in-hospital mortality, and total costs and charges. The University Hospitals Case Medical Center Institutional Review Board determined this study meets the exemption criteria for human subjects research (IRB #EM-14-30).

We identified all patients age 65 and older that had an emergency general surgery (EGS) procedures using ICD-9-CM procedure codes based on published procedure codes associated with the seven procedures: colon operations, small bowel operations, gallbladder operations, surgical treatment of peptic ulcer disease, lysis of peritoneal adhesions, appendectomy, and other laparotomy as described by Scott, et al.² We utilized both primary and secondary procedure codes to flag EGS procedures, and included only patients flagged as emergent.

Variables

We measured the presence of multiple comorbid conditions using the Elixhauser comorbidity index. The Elixhauser index contains 29 comorbid conditions defined through secondary ICD-9-CM diagnosis codes and DRG codes.⁸⁻¹⁰ Our main outcome variable of interest was in-hospital mortality, as recorded on the hospital billing record discharge status.

Other variables of interest included patient age, sex, race and ethnicity, and procedure type. Race was categorized into four categories white, black, Hispanic, and other/missing. Procedure type included the seven categories mentioned above. Age was grouped into 3 categories: 65–74, 75–84, and age over 85. Secondary outcomes analyzed included total length of stay, total cost, and discharge to a facility.

Analysis

Frequency counts and percentages were tabulated for all categorical outcomes. For descriptive analysis, we used discharge-level survey weights provided in the NIS and accounted for complex survey design effects. Trends for mortality were examined over age groups and procedure types. In addition, mean length of stay, costs, and rates of discharge to a facility were examined over the aforementioned age categories.

We used Association Rule Mining (ARM) to identify the most common single, dyad and triad combination of comorbid conditions, and to identify which of these combinations were most highly associated with in-hospital mortality.¹¹ ARM is a data mining method originally developed for consumer data to find items commonly purchased together in the same transaction, but has since been applied to a variety of applications in medicine and

bioinformatics.^{12,13} The ARM method can also be used to create “association rules” of the form $X \Rightarrow Y$, where X is one or more items, and Y is a single item consequent that X is associated with.

We apply the method treating each discharged individual as the “transaction” and the Elixhauser comorbidities as the “items” to find the most frequently co-occurring combinations. For each combination we also calculate the “lift” which is the ratio of the observed percentage of people with the combination divided by the expected percentage of people with that combination if each individual diagnosis was independent of one another.¹⁴ We then treated in-hospital mortality as the consequent to compute which of these combinations are most highly associated with in-hospital mortality. Our main measure of association was the adjusted odds ratio, calculated with multivariable logistic regression with in-hospital mortality as the dependent variable, the combination as the independent variable, and controlling for age, sex, race, and procedure type.

ARM uses the “Apriori” algorithm to search all possible combinations of conditions.¹⁵ As there are 2^k possible combinations where k is the number of possible items (in our study there are 29 comorbidities, so $2^{29} = 536,870,912$ possible combinations), usually some minimum frequency criteria is set to make the search computationally feasible. Because mortality occurs in less than 4% of EGS overall, we set a low minimum “Support” of 0.1% and a minimum confidence of 5%. Support is the measure of prevalence for that particular rule or combination in the population, and confidence is the proportion of times that the rule is true.¹⁵ Further, we set a minimum improvement criteria of 10% to filter out rules that are redundant or offer little new information over more parsimonious rules.¹⁶

All analyses were conducted using R version 3.5.1 and RStudio version 1.1.456, along with the “arules” package version 1.6–1¹⁷ and the “survey” package version 3.33–2.¹⁸

RESULTS

Overall, 280,885 patient encounters were identified with our inclusion criteria, with an overall mortality rate of 5.2%. Patient characteristics are presented in Table 1. There were more women than men across all three age categories, with the percentage increasing as age increased. The population includes substantial numbers of patients from minority race and ethnicity groups (25–30% across the three age groups). Most of the patients undergoing emergency surgery were direct admissions to that hospital, with less than ten percent transfers.

The most common comorbidities identified (Table 2) were hypertension, fluid and electrolyte disorders, cardiac arrhythmias, uncomplicated diabetes, and pulmonary disease. The percent with hypertension, fluid and electrolyte disorder, and cardiac arrhythmias increased as age increased. Conversely, the percent with uncomplicated diabetes and chronic pulmonary disease was lower among older patients.

Table 3 describes the primary and secondary outcomes of interest. Mortality by procedure type within the three age categories is described. Lengths of stay were similar (mean 8.8–9.4 days) across age categories for all age groups. Mortality rates increased substantially by age

group for most of the surgical types, with the oldest group having the highest mortality rates for all except vascular surgery, where the 75 to 84 age group had a mortality rate of 5.33% while the 85 and older group had a mortality rate of 5.22%.

As age group increased, the proportion of patients having ulcer, small bowel, colon, and adhesiolysis surgery increased, while patients having gallbladder, appendix, and other emergency laparotomy surgery decreased (Table 1). Mortality increased in all procedure types over the age groups (Table 3). Costs were similar between age groups. Discharge to a facility increased dramatically in the three age groups. For patients aged 65–74, discharge to a facility occurred in 17%, versus 29% in patients aged 75 to 84, and 46% in the oldest old.

The most frequently occurring two-way and three-way comorbidity combinations are reported in Table 4. For the top two-way combinations, hypertension was part of 8 of the top 10 combinations. The second most prevalent condition was fluid and electrolyte disturbance in three of the 10. For the three-way combinations, hypertension occurred in all the top ten comorbid combinations while deficiency anemia occurred in 4 of the top 10 combinations. The combination of hypertension & fluid/electrolyte disorders was the most common combination at 32.2% of the population, but the lift of 1.01 suggests this is not higher than expected. On the other hand, the combination of hypertension, arrhythmia, and congestive heart failure (7.2%) co-occurred 1.93 times higher than expected in the study population. Diseases that physiologically co-occur did have higher lift, for example diabetes and renal failure (lift 2.89, occurring in 2.4% of the cohort), and congestive heart failure and pulmonary circulation disorders (lift 3.01, occurring in 2.1% of the population). Note that these combinations are non-exclusive, so for instance, a person with seven comorbidities may appear in multiple two- or three-way groupings.

We list the one-way, two-way, and three-way combinations of comorbidities with the highest impact on mortality in Table 5. Coagulopathy was present in 8.3% of the study population, of whom 17.2% died in-hospital, with an adjusted odd ratio (aOR) of mortality was 3.74 (95% CI: [3.41 – 4.11]). Fluid and electrolyte disorders were associated with the second highest aOR (2.89, 95% CI: 2.66 – 3.14) for a single condition, which occurred in 44.1% of the population. The combination of Coagulopathy & Fluid and Electrolyte Disorders, present in 5.3% of the cohort, was associated with a 4.65 (95% CI: 4.20 – 5.15) times higher odds of mortality after adjustment, the highest of any two-way combination. The combination of Coagulopathy & Fluid and Electrolyte Disorders & Peripheral Vascular Disorders was associated with 5.10 (95% CI: 4.17 – 6.24) times higher odds of mortality after adjustment, the highest of any three-way combination.

DISCUSSION

Older patients represent a significant proportion of the emergency general surgery patients in the United States, and it is well documented that these patients face disproportionately high morbidity and mortality. Several theories have been proposed to explain the high risk of morbidity and mortality in our older surgical patients, including frailty, composite comorbidity scores, failure to rescue, and reluctance to pursue aggressive management.^{19–21} Additionally, several studies have reported that increasing age alone is an independent risk

factor for mortality, even when adjusted for comorbidities.²² Our study characterized the distribution of emergency general surgical conditions for the older patient population, as well as described the distribution and risk of mortality associated with individual comorbidities and comorbidity combinations.

Previous studies have suggested that a multitude of factors are associated with poor outcome, including American Society of Anesthesiologists class, cancer, hepatic disease, vascular disease, poor nutrition, hospital volume, insurance status, and income.^{6,23–26} Death from emergency surgery tends to be from organ failure that ensues in the post-operative setting, rather than as a direct sequelae of the index indication for surgery. As such, we hypothesized that the acute surgical disease and a patient's preexisting chronic conditions interact to create this burden. In our study, comorbidities and mortality both increase with age, suggesting that a patient's comorbidity burden is likely a large driver of mortality in this patient population. Furthermore, we demonstrated specific combinations of comorbidities associated with disproportionate mortality, suggesting that comorbidities do not contribute equally to mortality. Hypertension, the most common comorbidity, was not present in any of the high risk mortality combinations.

Our findings suggested that coagulopathy carries significant risk for postoperative death. Coagulopathy is a well-known risk factor for poor outcomes in some surgical conditions, particularly in trauma. Traumatic coagulopathy leads to both hemorrhagic shock associated death but also is associated with multiple organ failure.^{27–29} Coagulopathy is also associated with death in nontraumatic surgical settings, such as abdominal aortic aneurysm,³⁰ and is included in multiple well-used clinical scoring systems for critically ill patients such as the Sequential Organ Failure Assessment Score and the Multiple Organ Dysfunction Score. While coagulopathy is an important part of sepsis-related organ failure, on its own, it is not traditionally considered a major risk factor for postoperative death.^{31,32} Unfortunately, timing of the development of these comorbidities is impossible to determine within the Nationwide Inpatient Sample, as all diagnoses are coded at the time of discharge, and present on admission indicators are not available. These comorbidities may have been preexisting or may have developed after the admission. For example, the coding for coagulation disorders includes congenital and acquired coagulopathy, which includes coagulopathies secondary to hemorrhage, transfusion, vitamin deficiencies, medication administration, and multiple organ failure. Our study was unable to determine whether preoperative coagulopathy (for example warfarin use or von Willebrand disease) carries similar risk to pathologic coagulopathy from sepsis or multiple organ failure. Nevertheless, the effect size is large, with an adjusted odds ratio of 3.74 when considered alone, and higher when combined with other comorbidities such as fluid and electrolyte disorders and peripheral vascular disease. Based on these data, we believe that coagulopathy of any etiology likely carries a high risk of mortality, especially when combined with other comorbidities.

Additional limitations of this study should be considered, and are largely related to the administrative data. Comorbidities are subject to coding errors; therefore, some comorbidities may not have been captured. However, the NIS is commonly used to analyze complications and comorbidity patterns among hospitalized patients because of its large

sample size and all-payer national representativeness.^{33–36} Furthermore, this administrative database is limited by lack of clinical data and follow-up assessments so that no assessment could be made regarding severity of surgical illness, frailty or other geriatric syndromes, considerations made at the time of treatment, decisions regarding aggressiveness of care, or post-discharge morbidity, mortality and destination (i.e. home or a facility). We are also unable to study patients who had surgical conditions but declined surgical intervention. Additionally, lack of additional pertinent measures such as functional and cognitive status limits our ability to fully characterize a patient's multimorbidity.³⁷ However, for our purposes, the NIS was ideal for a large-scale population based analysis of comorbidities available through administrative coding of comorbidities and emergency surgical conditions.

Our findings have several important implications to clinical practice related to emergency surgery in older patients. First, we provide data of use to the clinician for important prognostic decisions in this patient population, as well as provide information on age-specific and disease category-specific outcomes. Second, we identified the most frequently co-occurring comorbidities within this population. Lastly, we identified the ten comorbidities, two-way combinations, and three-way combinations that portend the worst prognosis for patients undergoing EGS surgeries. We believe that it is important for clinicians to note that patients with coagulopathy and fluid and electrolyte disorders in the perioperative setting, in particular, may be at higher risk of death than other patients. Although further research is needed to explore whether these are pre-existing or consequential from their procedures, these physiologic derangements may be a “canary in the coal mine” for patients with a high risk of death.

Unfortunately, long-term functional outcomes are largely unknown for the population of older survivors of emergency surgery. Given older age and the common co-occurrence of multiple chronic conditions, these patients are already at risk for depletion of physiological and functional reserves, therefore loss of independence and decline in ability to perform activities of daily living. Nearly half of the patients over the age of 85 in our study were discharged to a nursing facility. Prior research suggests that these patients may have a slow postoperative decline to early death; one study by Cooper et al. found that 50% of patients aged 85 and older died within one year of EGS.³⁸ From a patient-and family-centered approach, there is interest in the longer-term outcomes, particularly for persons who may require an institutional stay after surgery. Further research is necessary to provide functional prognostication for patients and their families during these unplanned admissions.

CONCLUSION

EGS conditions represent a sudden and unexpected life event for older patients, who are at substantial risk of morbidity and mortality. The gravity of these conditions is compounded by the increasing presence of comorbid conditions in older patients. We identified specific combinations of comorbidities with the highest impact on mortality. In our data, the combination of coagulopathy, fluid and electrolyte disorders, and weight loss had the highest adjusted odds of death. As individuals live longer and healthier lives, and live healthier with more comorbidity, providers will encounter increasing numbers of older adults with EGS conditions. Due to the high mortality and morbidity of these diseases, increasing efforts

must be made to ensure personalized prognostication to allow for informed and shared decision making between patients, their families, and their caregivers. Future research must be directed towards further elucidating the risks associated with emergency general surgery in the older patient, as well as examine long-term and functional outcomes for this population.

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References:

1. Gale SC, Shafi S, Dombrovskiy VY, Arumugam D, Crystal JS. The public health burden of emergency general surgery in the United States: A 10-year analysis of the Nationwide Inpatient Sample--2001 to 2010. *The journal of trauma and acute care surgery* 8 2014;77(2):202–208. [PubMed: 25058242]
2. Scott JW, Olufajo OA, Brat GA et al. Use of National Burden to Define Operative Emergency General Surgery. *JAMA surgery* 4 27 2016:e160480. [PubMed: 27120712]
3. Massarweh NN, Legner VJ, Symons RG, McCormick WC, Flum DR. Impact of advancing age on abdominal surgical outcomes. *Arch. Surg* 12 2009;144(12):1108–1114. [PubMed: 20026827]
4. Ogola GO, Gale SC, Haider A, Shafi S. The financial burden of emergency general surgery: National estimates 2010 to 2060. *The journal of trauma and acute care surgery* 9 2015;79(3):444–448. [PubMed: 26307879]
5. Meraya AM, Raval AD, Sambamoorthi U. Chronic condition combinations and health care expenditures and out-of-pocket spending burden among adults, Medical Expenditure Panel Survey, 2009 and 2011. *Prev. Chronic Dis* 2015;12:E12. [PubMed: 25633487]
6. Shah AA, Haider AH, Zogg CK et al. National estimates of predictors of outcomes for emergency general surgery. *The journal of trauma and acute care surgery* 3 2015;78(3):482–490; discussion 490–481. [PubMed: 25710417]
7. 2011 Introduction to the NIS. Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality www.hcup-us.ahrq.gov/db/nation/nis/NIS_Introduction_2011.jsp. Accessed June 2016.
8. Southern DA, Quan H, Ghali WA. Comparison of the Elixhauser and Charlson/Deyo methods of comorbidity measurement in administrative data. *Med. Care* 4 2004;42(4):355–360. [PubMed: 15076812]
9. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med. Care* 1 1998;36(1):8–27. [PubMed: 9431328]
10. van Walraven C, Austin PC, Jennings A, Quan H, Forster AJ. A modification of the Elixhauser comorbidity measures into a point system for hospital death using administrative data. *Medical care* 6 2009;47(6):626–633. [PubMed: 19433995]
11. Agrawal R, Imielinski R, Swami A. Mining association rules between sets of items in large databases. *Proceedings of the 1993 ACM SIGMOD International Conference on Management of Data*; 1993, 1993; Washington, DC.

12. Held FP, Blyth F, Gnjjidic D et al. Association Rules Analysis of Comorbidity and Multimorbidity: The Concord Health and Aging in Men Project. *J. Gerontol. A Biol. Sci. Med. Sci* 5 2016;71(5): 625–631. [PubMed: 26508296]
13. Tai YM, Chiu HW. Comorbidity study of ADHD: applying association rule mining (ARM) to National Health Insurance Database of Taiwan. *Int. J. Med. Inform* 12 2009;78(12):e75–83. [PubMed: 19853501]
14. Brin S, Motwani R, Ullman JD, Tsur S. Dynamic itemset counting and implication rules for market basket data. *Proceedings of the 1997 ACM SIGMOD International Conference on Management of Data*; 1997, 1997; Tucson, AZ.
15. Agrawal R, Srikant R. Fast algorithms for mining association rules. *Proceedings of the 20th International Conference on Very Large Data Bases*; 1994; Santiago de Chile, Chile.
16. Bayardo RJ, Rakesh A, Gunopulos D. Constraint-Based Rule Mining in Large, Dense Databases. *Data Mining and Knowledge Discovery* 2000;4(2–3):217–240.
17. Hahsler M, Grun B, Hornik K. arules – A Computational Environment for Mining Association Rules and Frequent Item Sets. *Journal of Statistical Software* 2005;14(15):1–25.
18. Lumley T Analysis of Complex Survey Samples. *Journal of Statistical Software* 2004-04–15 2004;9(1):1–19.
19. Scarborough JE, Pappas TN, Bennett KM, Lagoo-Deenadayalan S. Failure-to-pursue rescue: explaining excess mortality in elderly emergency general surgical patients with preexisting “do-not-resuscitate” orders. *Ann. Surg* 9 2012;256(3):453–461. [PubMed: 22868360]
20. Orouji Jokar T, Ibraheem K, Rhee P et al. Emergency general surgery specific frailty index: A validation study. *The journal of trauma and acute care surgery* 8 2016;81(2):254–260. [PubMed: 27257694]
21. Mehta HB, Dimou F, Adhikari D et al. Comparison of Comorbidity Scores in Predicting Surgical Outcomes. *Med. Care* 2 2016;54(2):180–187. [PubMed: 26595225]
22. Bentrem DJ, Cohen ME, Hynes DM, Ko CY, Bilimoria KY. Identification of specific quality improvement opportunities for the elderly undergoing gastrointestinal surgery. *Arch. Surg* 11 2009;144(11):1013–1020. [PubMed: 19917937]
23. Hamel MB, Henderson WG, Khuri SF, Daley J. Surgical outcomes for patients aged 80 and older: morbidity and mortality from major noncardiac surgery. *J. Am. Geriatr. Soc* 3 2005;53(3):424–429. [PubMed: 15743284]
24. Ingraham AM, Cohen ME, Bilimoria KY et al. Comparison of 30-day outcomes after emergency general surgery procedures: potential for targeted improvement. *Surgery* 8 2010;148(2):217–238. [PubMed: 20633727]
25. Joseph B, Pandit V, Zangbar B et al. Superiority of frailty over age in predicting outcomes among geriatric trauma patients: a prospective analysis. *JAMA surgery* 8 2014;149(8):766–772. [PubMed: 24920308]
26. Arenal JJ, Bengoechea-Beeby M. Mortality associated with emergency abdominal surgery in the elderly. *Can. J. Surg* 4 2003;46(2):111–116. [PubMed: 12691347]
27. Maegele M, Lefering R, Yucel N et al. Early coagulopathy in multiple injury: an analysis from the German Trauma Registry on 8724 patients. *Injury* 3 2007;38(3):298–304. [PubMed: 17214989]
28. MacLeod JB, Lynn M, McKenney MG, Cohn SM, Murtha M. Early coagulopathy predicts mortality in trauma. *J. Trauma* 7 2003;55(1):39–44. [PubMed: 12855879]
29. Peltan ID, Vande Vusse LK, Maier RV, Watkins TR. An International Normalized Ratio-Based Definition of Acute Traumatic Coagulopathy Is Associated With Mortality, Venous Thromboembolism, and Multiple Organ Failure After Injury. *Crit. Care Med* 7 2015;43(7):1429–1438. [PubMed: 25816119]
30. Chen JC, Hildebrand HD, Salvian AJ et al. Predictors of death in nonruptured and ruptured abdominal aortic aneurysms. *J. Vasc. Surg* 10 1996;24(4):614–620; discussion 621–613. [PubMed: 8911410]
31. Sangji NF, Bohnen JD, Ramly EP et al. Derivation and validation of a novel Emergency Surgery Acuity Score (ESAS). *The journal of trauma and acute care surgery* 8 2016;81(2):213–220. [PubMed: 27032007]

32. Bilimoria KY, Liu Y, Paruch JL et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: a decision aid and informed consent tool for patients and surgeons. *J. Am. Coll. Surg* 11 2013;217(5):833–842.e831–833. [PubMed: 24055383]
33. Chitale R, Campbell PG, Yadla S et al. International classification of disease clinical modification 9 modeling of a patient comorbidity score predicts incidence of perioperative complications in a nationwide inpatient sample assessment of complications in spine surgery. *Journal of spinal disorders & techniques* 5 2015;28(4):126–133. [PubMed: 22960417]
34. Menendez ME, Ring D. A Comparison of the Charlson and Elixhauser Comorbidity Measures to Predict Inpatient Mortality After Proximal Humerus Fracture. *J. Orthop. Trauma* 11 2015;29(11):488–493. [PubMed: 26165266]
35. Lee CS, Chien CV, Bidwell JT et al. Comorbidity profiles and inpatient outcomes during hospitalization for heart failure: an analysis of the U.S. Nationwide inpatient sample. *BMC Cardiovasc. Disord* 2014;14:73. [PubMed: 24898986]
36. Kapoor A, Labonte AJ, Winter MR et al. Risk of venous thromboembolism after total hip and knee replacement in older adults with comorbidity and co-occurring comorbidities in the Nationwide Inpatient Sample (2003–2006). *BMC Geriatr* 2010;10:63. [PubMed: 20846450]
37. Koroukian SM, Warner DF, Owusu C, Given CW. Multimorbidity redefined: prospective health outcomes and the cumulative effect of co-occurring conditions. *Prev. Chronic Dis* 2015;12:E55. [PubMed: 25906436]
38. Cooper Z, Mitchell SL, Gorges RJ et al. Predictors of Mortality Up to 1 Year After Emergency Major Abdominal Surgery in Older Adults. *J. Am. Geriatr. Soc* 12 2015;63(12):2572–2579. [PubMed: 26661929]

Table 1:

Patient Characteristics

Patient Characteristics	Age (65 – 74)		Age (75 – 84)		Age over 85	
	n	%	n	%	n	%
Total Subjects	130,280		101,560		49,045	
Sex						
Female	66,770	51.3	53,265	52.4	29,445	60.0
Male	63,510	48.7	48,295	47.6	19,600	40.0
Race						
White	93,105	71.5	75,375	74.2	37,700	76.9
Black	12,700	9.7	8,120	8.0	3,190	6.5
Hispanic	10,710	8.2	7,800	7.7	3,160	6.4
Other/Missing	13,765	10.6	10,265	10.1	4,995	10.2
Insurance						
Medicare	108,840	83.5	92,995	91.6	45,935	93.7
Medicaid	2,650	2.0	1,415	1.4	410	0.8
Private	16,145	12.4	5,700	5.6	2,220	4.5
Other	2,510	1.9	1,380	1.4	425	0.9
Transfer status						
Transfer in	11,415	8.8	9,430	9.3	4,645	9.5
Hospital Type						
Urban, Teaching	11,630	8.9	9,200	9.1	4,320	8.8
Urban, Non-Teaching	40,640	31.2	32,245	31.7	15,975	32.6
Rural	78,010	59.9	60,115	59.2	28,750	58.6
Hospital region						
Northeast	23,750	18.2	19,365	19.1	10,130	20.7
Midwest	27,560	21.2	22,860	22.5	11,865	24.2
South	51,410	39.5	38,680	38.1	16,815	34.3
West	27,560	21.2	20,655	20.3	10,235	20.9
Hospital bed size						
Small	23,565	18.1	18,005	17.7	9,425	19.2
Medium	39,585	30.4	31,905	31.4	15,815	32.2
Large	67,130	51.5	51,650	50.9	23,805	48.5
Procedure Type						
Colon Surgery	19,710	15.1	16,585	16.3	8,305	16.9
Small Bowel Surgery	13,295	10.2	11,480	11.3	6,375	13.0
Gallbladder Surgery	46,975	36.1	33,915	33.4	13,820	28.2
Ulcer Disease	23,660	18.2	23,205	22.8	13,395	27.3
Lysis of Adhesions	26,750	20.5	21,410	21.1	10,750	21.9
Appendectomy	12,650	9.7	6,185	6.1	2,120	4.3
Laparotomy	7,280	5.6	5,015	4.9	2,005	4.1

Table 2:

Prevalence of Comorbidities

Comorbidities	All Patients		Age (65 – 74)		Age (75 – 84)		Age over 85	
	N	%	n	%	n	%	n	%
Total Cohort	280,885		130,280		101,560		49,045	
Comorbidity								
Hypertension	202,525	72.1	88,630	68.0	76,095	74.9	37,800	77.1
Fluid and Electrolyte Disorders	123,745	44.1	52,450	40.3	46,480	45.8	24,815	50.6
Cardiac Arrhythmias	93,190	33.2	32,010	24.6	38,215	37.6	22,965	46.8
Diabetes - Uncomplicated	66,915	23.8	32,655	25.1	25,130	24.7	9,130	18.6
Chronic Pulmonary Disease	61,720	22.0	28,585	21.9	23,635	23.3	9,500	19.4
Deficiency Anemias	56,915	20.3	23,535	18.1	21,485	21.2	11,895	24.3
Renal Failure	51,905	18.5	18,370	14.1	21,310	21.0	12,225	24.9
Hypothyroidism	45,920	16.3	17,520	13.4	17,615	17.3	10,785	22.0
Congestive Heart Failure	44,800	15.9	14,485	11.1	18,425	18.1	11,890	24.2
Weight Loss	41,705	14.8	17,020	13.1	15,715	15.5	8,970	18.3
Obesity	35,590	12.7	22,245	17.1	10,920	10.8	2,425	4.9
Peripheral Vascular Disorders	32,835	11.7	12,980	10.0	13,115	12.9	6,740	13.7
Depression	26,365	9.4	13,445	10.3	8,925	8.8	3,995	8.1
Coagulopathy	23,345	8.3	9,930	7.6	8,940	8.8	4,475	9.1
Valvular Disease	23,060	8.2	6,945	5.3	9,530	9.4	6,585	13.4
Other Neurological Disorders	20,430	7.3	7,860	6.0	8,035	7.9	4,535	9.2
Metastatic Cancer	13,780	4.9	6,735	5.2	4,995	4.9	2,050	4.2
Liver Disease	13,115	4.7	8,105	6.2	3,960	3.9	1,050	2.1
Diabetes – Chronic Complications	12,740	4.5	6,395	4.9	4,775	4.7	1,570	3.2
Pulmonary Circulation Disorders	12,375	4.4	4,370	3.4	4,845	4.8	3,160	6.4
Chronic Blood Loss Anemia	10,755	3.8	4,175	3.2	4,210	4.1	2,370	4.8
Rheumatoid Arthritis	9,520	3.4	4,365	3.4	3,700	3.6	1,455	3.0
Solid Tumor without Metastasis	8,990	3.2	3,920	3.0	3,475	3.4	1,595	3.3
Alcohol Abuse	7,740	2.8	5,260	4.0	2,095	2.1	385	0.8
Psychoses	7,645	2.7	4,175	3.2	2,460	2.4	1,010	2.1
Paralysis	5,380	1.9	2,655	2.0	1,855	1.8	870	1.8
Lymphoma	2,970	1.1	1,310	1.0	1,160	1.1	500	1.0
Drug Abuse	2,005	0.7	1,425	1.1	450	0.4	130	0.3
Peptic Ulcer Disease	385	0.1	210	0.2	120	0.1	55	0.1
AIDS	150	0.1	125	0.1	25	0.0	0	0

Table 3:

Outcomes after Emergency General Surgery

Outcome	Age (65 – 74)		Age (75 – 84)		Age over 85	
	n	%	n	%	n	%
Mortality						
Entire Cohort	5530	4.2	6250	6.2	3980	8.1
Colon Surgery	1840	9.3	2080	12.5	1265	15.2
Small Bowel Surgery	1365	10.2	1450	12.6	960	15.1
Gallbladder Surgery	535	1.1	565	1.7	420	3.0
Ulcer Disease	1015	4.3	1270	5.5	850	6.4
Lysis of Adhesions	1305	4.9	1600	7.5	1005	9.4
Appendectomy	55	0.5	125	2.0	70	3.3
Laparotomy	1435	19.7	1265	25.2	625	31.2
Length of Stay (mean, SD)	8.8	10.1	9.3	9.2	9.4	7.5
Discharge to Facility (n, %)	22,285	17.10	29,555	29.10	22,420	45.70
Total Cost, \$ (mean, SD)	25,253	32,770	25,144	28,130	23,800	21,388

Table 4.

Two-Way and Three-Way Comorbidity Combinations with the Highest Prevalence

Diagnosis 1	Diagnosis 2	Diagnosis 3	Lift	Percent
2-way combinations				
Hypertension-Combine	Fluid and Electrolyte Disorders		1.014	32.2
Hypertension-Combine	Arrhythmias		1.061	25.4
Diabetes-Uncomplicated	Hypertension-Combine		1.167	20.1
Fluid and Electrolyte Disorders	Arrhythmias		1.168	17.1
Chronic Pulmonary Disease	Hypertension-Combine		1.034	16.4
Hypertension-Combine	Renal Failure		1.221	16.3
Deficiency Anemias	Hypertension-Combine		1.069	15.6
Hypertension-Combine	Hypothyroidism		1.062	12.5
Congestive Heart Failure	Hypertension-Combine		1.068	12.3
Deficiency Anemias	Fluid and Electrolyte Disorders		1.287	11.5
3-way combinations				
Hypertension-Combine	Fluid and Electrolyte Disorders	Arrhythmias	1.223	12.9
Deficiency Anemias	Hypertension-Combine	Fluid and Electrolyte Disorders	1.374	8.8
Diabetes-Uncomplicated	Hypertension-Combine	Fluid and Electrolyte Disorders	1.157	8.8
Hypertension-Combine	Fluid and Electrolyte Disorders	Renal Failure	1.454	8.5
Chronic Pulmonary Disease	Hypertension-Combine	Fluid and Electrolyte Disorders	1.103	7.7
Congestive Heart Failure	Hypertension-Combine	Arrhythmias	1.932	7.4
Hypertension-Combine	Renal Failure	Arrhythmias	1.639	7.2
Hypertension-Combine	Fluid and Electrolyte Disorders	Weight Loss	1.453	6.9
Diabetes-Uncomplicated	Hypertension-Combine	Arrhythmias	1.197	6.8
Chronic Pulmonary Disease	Hypertension-Combine	Arrhythmias	1.26	6.6

Caption: Lift is the ratio of the observed number (or percentage) of people with the combination divided by the expected number (or percentage) of people with that combination if each individual diagnosis was independent of one another. For a two-way combination this is calculated as $P(dx1 \& dx2) / [P(dx1)*P(dx2)]$, and for three-way it is calculated as $P(dx1 \& dx2 \& dx3) / [P(dx1)*P(dx2)*P(dx3)]$, where dx1, dx2, and dx3 are individual comorbidity diagnoses. Note: the order of the conditions (diagnosis 1, diagnosis 2, or diagnosis 3) in the combination does not matter.

Table 5:

One-way, Two-way, and Three-way Comorbidity Combinations with the Highest Impact on Mortality

Combination of comorbidities	Percent with Combination (Coverage)	Percent died in-hospital (Confidence)	Odds Ratio	Adjusted Odds Ratio	95% Confidence Interval
One-way combination					
Coagulopathy	8.3%	17.2%	4.35	3.74	3.41–4.11
Fluid and Electrolyte Disorders	44.1%	9.4%	3.89	2.89	2.66–3.14
Liver Disease	4.7%	7.2%	1.32	1.89	1.61–2.22
Weight Loss	14.8%	11.9%	2.86	1.84	1.70–2.01
Peripheral Vascular Disorders	11.7%	10.5%	2.24	1.82	1.66–2.00
Paralysis	1.9%	10.3%	1.97	1.78	1.44–2.19
Congestive Heart Failure	15.9%	9.4%	2.03	1.74	1.59–1.90
Arrhythmias	33.2%	8.4%	2.09	1.73	1.60–1.86
Pulmonary Circulation Disorders	4.4%	9.8%	1.89	1.65	1.43–1.91
Renal Failure	18.5%	8.1%	1.66	1.53	1.40–1.67
Two-way combination					
Coagulopathy & Fluid and Electrolyte Disorders	5.3%	22.4%	5.91	4.65	4.20–5.15
Coagulopathy & Peripheral Vascular Disorders	1.4%	24.5%	5.76	4.21	3.52–5.04
Liver Disease & Weight Loss	0.7%	18.1%	3.77	3.71	2.84–4.85
Coagulopathy & Arrhythmias	3.7%	19.1%	4.40	3.64	3.22–4.12
Coagulopathy & Chronic Pulmonary Disease	1.9%	19.0%	4.16	3.58	3.03–4.23
Coagulopathy & Weight Loss	2.2%	21.4%	4.89	3.37	2.90–3.92
Fluid and Electrolyte Disorders & Liver Disease	2.1%	13.1%	2.61	3.09	2.56–3.72
Fluid and Electrolyte Disorders & Peripheral Vascular Disorders	6.0%	16.0%	3.67	2.61	2.35–2.90
Fluid and Electrolyte Disorders & Paralysis	1.1%	14.5%	2.91	2.43	1.90–3.10
Fluid and Electrolyte Disorders & Arrhythmias	17.1%	12.2%	3.13	2.37	2.19–2.56
Three-way combination					
Coagulopathy & Fluid and Electrolyte Disorders & Peripheral Vascular Disorders	1.0%	30.2%	7.62	5.10	4.17–6.24
Coagulopathy & Fluid and Electrolyte Disorders & Chronic Pulmonary Disease	1.3%	25.0%	5.89	4.83	4.00–5.82
Fluid and Electrolyte Disorders & Liver Disease & Weight Loss	0.5%	21.6%	4.71	4.43	3.30–5.97
Coagulopathy & Chronic Pulmonary Disease & Arrhythmias	1.0%	21.2%	4.65	3.89	3.10–4.87
Coagulopathy & Congestive Heart Failure & Chronic Pulmonary Disease	0.7%	21.2%	4.61	3.81	2.91–5.00

Combination of comorbidities	Percent with Combination (Coverage)	Percent died in-hospital (Confidence)	Odds Ratio	Adjusted Odds Ratio	95% Confidence Interval
Coagulopathy & Congestive Heart Failure & Weight Loss	0.6%	24.1%	5.43	3.61	2.73–4.78
Fluid and Electrolyte Disorders & Liver Disease & Arrhythmias	0.7%	15.8%	3.20	3.49	2.60–4.67
Fluid and Electrolyte Disorders & Peripheral Vascular Disorders & Arrhythmias	2.7%	18.3%	4.05	2.88	2.49–3.31
Fluid and Electrolyte Disorders & Peripheral Vascular Disorders & Renal Failure	1.9%	18.0%	3.87	2.87	2.42–3.40
Fluid and Electrolyte Disorders & Pulmonary Circulation Disorders & Renal Failure	0.8%	15.9%	3.24	2.77	2.13–3.62

Coverage = percentage of population with that combination

Confidence = percentage of population that have the outcome (i.e. died in-hospital), among those with the combination

Adjusted Odds Ratio calculated with multivariable logistic regression, adjusted for all variables in Table 1. The p-value from the Wald test for all odds ratios and adjusted odds ratios presented in the table is $p < 0.001$.