Abstract Title: Phenotyping patients undergoing colectomy to anticipate clinical trajectory

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Background High-risk surgeries account for 12% of the cases performed but represent 80% of the postoperative mortality [1]. The ASA (*American Society of Anesthesiology*) score, used since 1941, categorizes risk based on patient's comorbidities [2]. Such stratification is of utmost importance, enabling therapeutic decision making, distribution of resources, decision sharing with patients, and billing. By exploiting clinical databases, risk scores could become automatically extracted from medical records, personalized for different populations, and quickly provide insights on several outcomes. By clustering a population with unsupervised artificial intelligence (AI) algorithms, we can create subgroups without specifying how to subdivide them. By identifying discriminative features, the AI creates subgroups from which we extract the typical profile, or phenotype, before describing the associated outcomes [3]. This recent approach identified subgroups among covid-19 and septic patients [3, 4]. The objective of this project is to export this concept for the first time to a surgical population and, considering the democratization of "*Enhanced Recovery after Surgery*" protocol, to identify phenotypes and associated outcomes in a population undergoing colectomy [5].

Methods Using the patient data warehouse (PDW) from University of California in Los Angeles (UCLA), we retrospectively extracted all surgical cases containing "colectomy" in the procedure name, which occurred between 2013, inception of the database, and November 2021 [6]. Institutional Review Board of UCLA waived the need for patient's consent. We selected 56 relevant variables, including demographic data, comorbidities, and medication. Unsupervised K-means clustering was applied to the data, and the optimal number of phenotypes was determined based on discrimination of significant binary outcomes, including mortality, intensive care unit (ICU) length of stay (LOS) over 10 days, and hospital LOS over 20 days. Continuous data, including age and preoperative vitals were normalized with a min-max algorithm before clustering. A random forest plot algorithm was used to identify the 15 most relevant features linked to mortality and compare the clustering results in a restricted set.

Results We identified three major phenotypes in the population (N=2273) based on the major characteristics described in Table 1, with an overall mortality of 0.08%. Despite being younger (average age: 52), phenotype 1 had the highest in-hospital mortality risk with 3.4% (15/437) and had longer ICU LOS (10.1% stayed > 10d), and hospital LOS (26.7% stayed >20d). This subgroup mostly contained patients undergoing urgent surgery (90%) with intestine obstruction (26%). While phenotypes 2 and 3 both were elective and included most cancer cases, mortality and LOS varied significantly between groups (mortality: 0.06% vs 2.1%; ICU>10d: 0.5% vs 7.2%; hospital LOS>20d: 2.4% vs 11.3%). Phenotype 2 was generally younger (57 vs 62 years old) and presented less comorbidities (see Figure 1). Cases lengths were similar across all groups, and phenotype 3 received more intravenous fluids. In this cohort, phenotype 1 (19.5% of procedures) accounted for 83.3% of deaths, 74,5% of prolonged ICU LOS, and 68,4% of prolonged hospital LOS. Clustering on the restricted feature built after random forest plot algorithm provided similar results.

Discussion and conclusion By identifying 3 phenotypes in the colectomy population, we could discriminate patients' outcome and trajectory of care. We confirmed that despite having few comorbidities, the highest risk of complication and prolonged ICU/hospital LOS correlates with urgent surgeries. In other words, urgency seems more correlated to adverse outcomes than comorbidities or ASA score. These results confirm the effectiveness of clustering the surgical population for risk stratification. While these analyses were limited by the low number of deaths, LOS insights were of great interest. Accumulating more data will be interesting to further phenotype patients undergoing urgent colectomy, or to personalize risk stratification for other surgeries.

Table 1. Summary statistics for the key covariates and clinical outcomes across phenotypes.

	Phenotype 1 N= 437	Phenotype 2 N= 1739	Phenotype 3 N= 97
Hospital Mortality	15 (3.4%)	1 (0.1%)	2 (2.1%)
ICU LOS > 10 d	44 (10.1%)	8 (0.05%)	7 (7.2%)
Hospital LOS > 30d	117	43	11
Age (mean)	53.7	57.5	62.2
Sex (Male)	49.9%	51.1%	50.5%
Weight (mean)	68.5 kg	74.8 kg	75.5 kg
Elective case	10.1%	98.4%	77.3%
Abdominal Obstruction	26.1%	0.8%	0.8%
Malignant intestine neoplasia	8.9%	27.2%	26.8%
Obesity (IMC >30)	0.1%	2.9%	13.4%
Hypertension	1.8%	0.9%	38.1%
Diabetes	3.6%	5.8%	10.3%
Smoking	0.7%	5.4%	8.2%
Ischemic heart disease	2.1%	2.9%	20.6%
Length of case	296 min	307 min	299 min
Crystalloid received	657 mL	739 mL	916 mL
Colloid received	169 mL	120 mL	156 mL

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