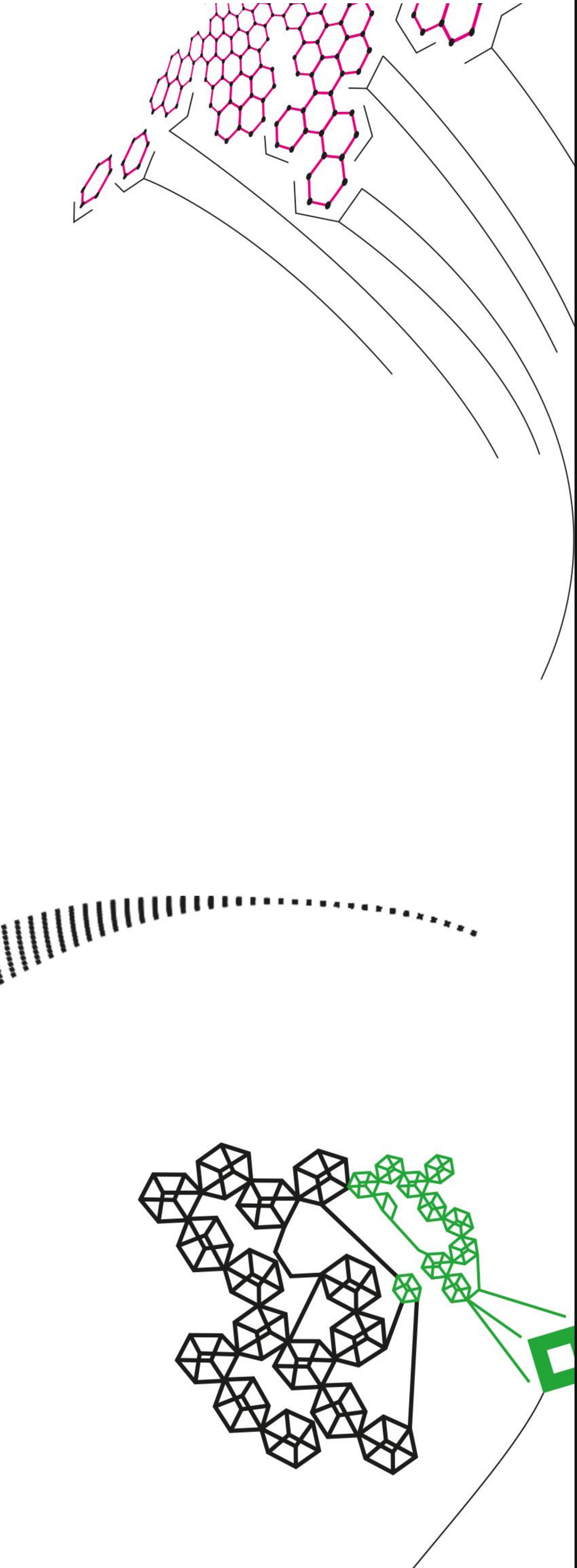

PREDICTING LENGTH OF STAY AFTER NEPHRECTOMY WITHIN THE ERAS PROGRAM

Medisch Spectrum Twente

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ABSTRACT

Introduction and Aims To study the preoperative patient characteristics, operation procedure and lesion variables, questionnaires and lab values associated with length of stay (LOS) after nephrectomy or nephroureterectomy in renal patients within the Enhanced Recovery After Surgery (ERAS) program.

Method A retrospective study of patients who underwent a robot-assisted partial or radical nephrectomy or robot-assisted nephroureterectomy. In total, 210 ERAS patients were included between April 2021 and March 2023. Short LOS is defined as shorter or equal to one night and a long LOS is more than one night. Comparisons were made between the short LOS group and the long LOS group using the T-test or the Chi-squared test. MICE imputations were used to impute missing data and a conditional forward stepwise variable selection was used to set up the multivariate logistic regression for the predictive model for LOS. The Area Under the Curve was used to assess the performance of the model. A Hosmer-Lemeshow goodness-of-fit test was used to test the model fit, and validation was done by using K-fold cross-validation in combination with a calibration plot.

Setting Value-Based Healthcare (VBHC) and Urology department, Medisch Spectrum Twente (MST), Enschede, the Netherlands.

Results Of the 210 patients there were 93 patients with a short LOS and 117 patients with a long LOS. Six variables, including ‘Procedure & Lesion size’, pulmonary disease, dyspnoea, GFR, smoking and MET-score, were selected in the multivariate logistic regression model. The predictive model demonstrated good discriminative power with an Area Under the Curve (AUC)-value of 0.79, indicating strong predictive ability. The Hosmer-Lemeshow goodness-of-fit resulted in a p-value of 0.96, which shows an adequate prediction. K-fold cross-validation yielded an accuracy of 67.8% and Cohen’s kappa statistic of 0.34, suggesting fair agreement between observed and predicted classifications. Furthermore, the calibration plot showed excellent calibration of the model.

Conclusion Based on the findings in this study, the predictive preoperative variables associated with LOS for renal patients undergoing nephrectomies are identified. The integration of predictive models could facilitate personalized care plans by providing patients with insights into factors affecting their LOS, thereby aiding in their preoperative preparation and postoperative recovery. For policymakers and planners, the predictive model could also be used in the facilitating of healthcare resources.

Keywords Enhanced Recovery After Surgery (ERAS), Length of Stay (LOS), nephrectomy, nephroureterectomy, urology, renal surgery, Value Based Healthcare (VBHC), Medisch Spectrum Twente (MST), multiple logistic regression model.

TABLE OF CONTENT

LIST OF ABBREVIATIONS

Abbreviation	**Definition**
AUC	Area Under the Curve
ASA	American Society of Anaesthesiologist
BMI	Body Mass Index
CI	Confidence Interval
eGFR	estimated Glomerular Filtration Rate
EIAS	ERAS Interactive Audit System
ERAS	Enhanced Recovery After Surgery
Hb	Haemoglobin
KATZ-ADL	Katz index of independence in Activities of Daily Living
LOS	Length Of Stay
MET	Metabolic Equivalent of Task
MDR	Medical Device Regulation
MST	Medisch Spectrum Twente
MICE	Multivariate Imputation by Chained Equations
OR	Odds Ratio
RCC	Renal cell carcinoma
SNAQ	Short Nutritional Assessment Questionnaire
VHBC	Value-Based HealthCare

1. INTRODUCTION

Since March 2020 Medisch Spectrum Twente (MST) implemented the Enhanced Recovery After Surgery (ERAS) program, a program proven to lead to better recovery after surgery [1][2]. The ERAS Society has designed many perioperative care pathways to achieve early recoveries for patients undergoing major surgeries [3]. The ERAS Society's procedure-specific pathway guidelines consist of around 20-25 interventions (elements or components) spread across the preoperative, intraoperative, and postoperative periods. MST is dedicated to delivering the highest quality and most efficient care. With the implementation of the ERAS program in 2020, MST can offer a perioperative care pathway to facilitate early recovery for patients undergoing major surgery [3].

As ERAS is already enrolled in different fields of care, some lessons could be learned from them. For example, in colorectal cancer surgery, the length of stay (LOS) was reduced by 30 to 50% after implementing the ERAS program [4]. Also proven is that the preoperative ERAS guidelines decrease anxiety, improve pain control and improve patient-reported outcomes measures [5]. The ERAS protocols are currently implemented in the intestinal, gynaecological, renal, pancreatic, and lung surgeries within the MST. For urology, there is no specific existing ERAS guideline for renal surgery yet. Despite this gap, the established radical cystectomy ERAS guideline can be applied to relevant aspects of renal surgery [6].

In the Netherlands renal cancer is a significant and increasing public health concern [7]. Renal cell carcinoma (RCC) affects approximately 400.000 patients annually, making it the seventh most prevalent neoplasm worldwide In the Netherlands over 2.600 patients get diagnosed with RCC every year [8]. The incidence of renal cancer is expected to increase by 31% in 2032 compared to 2019, resulting in higher care demand and rising costs [9]. Among the most established risk factors for developing renal cancer are cigarette smoking, obesity and hypertension, while poor dietary habits and inadequate physical activity also contribute to the risk of renal cancer [10][11]. Besides renal cancer, various conditions can also be a reason to undergo renal surgery. These include, for example, a poorly developed kidney, kidney trauma, a kidney abscess or cyst, kidney stones, shrivelling or chronic inflammation of the kidneys [12].

This study is a follow-up to a previous study conducted by S. Elferink (2023) [13]. Elferink et al. found numeric improvements in various components and a significant positive effect on LOS within the ERAS program after elective renal surgery on a textbook outcome (TO). Where the TO was described as a patient with a maximum of two nights in the hospital and no severe complications during or after surgery (≥ grade IIIb according to the Clavien-Dindo classification) [14]. The implementation of the ERAS protocols resulted in a higher incidence of the TO ERAS group (TO=76.8%) compared to the pre-ERAS group (TO=59.1%).

ERAS has resulted in a shorter LOS after major surgeries in the MST, this positive outcome prompts further investigation into the specific factors that contribute to the significant reduction in LOS after renal surgery. The variance in patient characteristics within a population, coupled with the components within the ERAS program, can result in differences in LOS [15]. Efficient management of preoperative interventions could lead to fewer postoperative complications and improved recoveries [16]. Therefore, the focus in determining parameters is on factors that can be determined before surgery. Currently, there is insufficient research to determine which preoperative patient characterisation, operation procedure and lesion-specific variables, questionnaire outcomes or lab values are associated with LOS [17]. The research question is therefore as follows:

‘Which preoperative patient characteristics, operation procedure and lesion-specific variables, questionnaire outcomes or lab values can contribute to predicting length of stay in renal patients undergoing robot-assisted partial nephrectomy, radical nephrectomy or nephroureterectomy in Medisch Spectrum Twente within the Enhanced Recovery After Surgery program?’

This research aims to answer the existing knowledge gap by identifying associated variables and formulating recommendations to optimize the care pathway for renal surgery patients, specifically targeting changes that can lead to shorter LOS. Additionally, it seeks to provide valuable pre-operative insights for patients regarding potential hospital stay duration, serving as a guide for both patients and healthcare professionals in postoperative planning. The goal is to visualize the predictive model, creating a tool that healthcare professionals can utilize in preoperative counselling. This model empowers patients to understand the steps necessary for favourable postoperative outcomes, enhancing patient engagement and informed decision-making.

2. METHODOLOGY

2.1 STUDY DESIGN AND DATA COLLECTION

This study is a quantitative retrospective patient record study and took place at the department ‘Value Based Healthcare’ within MST. Identifying the possible predictive parameters is accomplished through literature research and expert opinions. The key factors outlined in the ERAS guidelines, along with crucial patient characteristics, will serve as the foundation for further analysis. All the patients included in this study are treated confirm the ERAS guideline Urology [2][6].

The data related to the ERAS guidelines is saved in a database called ERAS Interactive Audit System (EIAS) [18]. Lab values and questionnaires were captured from the electronic patient record HiX.

Due to the nature of this study, no actions or behaviours were imposed on the patients, therefore no ethical approval or informed consent was needed under Dutch law. The procedure of this study (niet-WMO) is checked and confirmed by the Advisory Committee Medisch Spectrum Twente, Enschede (K23-48).

2.2 PATIENT POPULATION

Since the implementation of ERAS in the urology department in April 2021, and with EIAS capturing all data until March 2023, patients within this timeframe were included in the cohort group. The analysis comprised robotic-assisted radical nephrectomies, partial nephrectomies, and nephroureterectomies.

2.3 LENGTH OF STAY

According to the ERAS society, LOS is defined as the number of nights spent in the hospital after major surgery. This metric excludes readmissions, and the maximum follow-up time is 30 days. The ERAS guidelines aim for patients to continue their recovery outside the hospital within 1 night after surgery. LOS was therefore recoded into a dichotomous outcome measure with two categories: short length of stay (LOS ≤ 1 night) or long length of stay (LOS > 1 night) [19][20].

2.4 PREDICTIVE VARIABLES

Patient characterisation

The demographic factors of the patients, essential for characterization, encompass age (coded as a continuous variable), gender (male or female), and Body Mass Index (BMI) (coded into three categories: normal weight (BMI ≤ 25), overweight (BMI 25-30), and obese (BMI > 30)) [21][22]. Diabetes mellitus, severe pulmonary disease, and severe heart disease were assessed for presence in the category comorbidities, indicated by a binary classification as 'yes' or 'no' [23]. The usage of alcohol and drugs and the smoking behaviour of patients were recorded in EIAS. For all variables, there are three options: Yes, No, or Stopped because of surgery. However, the termination details are not consistently clear. Therefore, all patients who reported stopping within 4 weeks of the operation were coded as ‘Yes’ and otherwise as ‘No’ [24].

Operation procedure and lesion-specific variables

The operation procedure is categorized into partial nephrectomy, radical nephrectomy, and nephroureterectomy. Lesion size is categorized into three groups: lesions less than 4cm, lesions between 4 and 9 cm and lesions larger than 9 cm. In addition to lesion-specific variables, it is important to note that some patients in the population do not have lesions. For these patients, a value of zero is assigned for lesion size. Laterality is classified as left, right, or bilateral, while sub-location includes categories such as upper pole, central, lower pole, overlap, or whole kidney. Given that lesion size significantly influences the choice of surgical procedure, there is a strong interconnection between lesion size and the selected operation procedure [25]. Consequently, these two variables are integrated and analysed as one variable in the study to comprehensively assess their impact on surgical outcomes (Table 1).

Table 1: variable defining 'Procedure & Lesion size'

Procedure & Lesion size
Partial & lesion size < 4cm
Partial & lesion size ≥ 4cm
Radical & lesion size < 9cm
Radical & lesion size ≥ 9cm
Nephroureterectomy

Questionnaire outcomes

The questionnaires included in the study were: the Short Nutritional Assessment Questionnaire -score (SNAQ), Katz index of independence in Activities of Daily Living -score (KATZ-ADL), Metabolic Equivalent of Task -score (MET), and the dyspnoea-score [26][27][28][29]. In addition to these questionnaires the ASA-classification is also added to this category [30]. Table 2 is a schematic overview of the coding scheme for all the questionnaires.

Table 2: coding scheme questionnaires

Questionnaire	**Value**	**Function code**
SNAQ-score	0 points	Good nutritional status
	≥ 1 points	Moderate/poor nutritional status
KATZ-ADL-score	0 points	Independent
	≥ 1 points	Dependent
Dyspnoea-score	0 points	No dyspnoea
	≥ 1 points	Dyspnoeatic
MET-score	< 4 points	Poor condition
	≥ 4 points	Good condition
ASA-class	1 or 2	Group 1&2
	3 or 4	Group 3&4

Lab values

Distinguishing values in laboratory tests are based on preoperative haematocrit values, haemoglobin (Hb) levels and creatinine (Table 3). Closely tied to renal surgery is the measurement of kidney function, assessed through the Glomerular Filtration Rate (GFR). A recoding model, contingent on age and gender, was applied to this specific variable (Table 3: coding scheme lab values).

Table 3: coding scheme lab values

Laboratory test	Value	Function code
Haematocrit	Males: 0.41 – 0.51 L/L Females: 0.36 – 0.46 L/L	Normal range
	Males <0.41 and >0.51 Females <0.36 and >0.46	Outside normal values
Haemoglobin (Hb)	< 6 mmol/L	Low
	> 6 mmol/L and < 7,5 or 8,5	Moderate
	Females ≥ 7,5mmol/L Males ≥ 8,5mmol/L	Good
Creatinine	Males > 100 µmol/L Females > 80 µmol/L	Too high
	Males ≤ 100 µmol/L Females ≤ 80 µmol/L	Good
eGFR	All GFRs below 40%	Poor
	All GFRs >40% and <cutoff value	Moderate
	Females: GFR >85 (up to 40 years) GFR >75 (up to 50 years) GFR >70 (up to 60 years) GFR >50 (up to 70 years) GFR >40 (older than 70) *Males:* GFR >90 (up to 40 years) GFR >80 (up to 50 years) GFR >75 (up to 60 years) GFR >60 (up to 70 years) GFR >40 (older than 70)	Good

2.5 STATISTICAL ANALYSIS

All data analyses are conducted using RStudio version 4.1.2 (2023). With the dichotomous outcome measure in place, the statistical analysis will follow a stepwise logistic regression method.

Missing data may arise as missing at random or missing not at random. In instances of non-randomly missing data, manual recoding was performed to address the absence of certain variables. Specifically, for the SNAQ-score, KATZ-ADL-score, and dyspnoea-score, missing data were found to be correlated with specific outcomes. Consequently, the values of 'Good nutritional status,' 'Independent,' and 'No dyspnoea' were assigned to these variables respectively. This decision was made based on the assumption that when data was missing, it likely occurred because the corresponding questionnaires were skipped, indicating a lack of suspicion regarding adverse outcomes. For randomly missing data, Multivariate Imputation by Chained Equations (MICE) in RStudio was applied [31]. MICE is used to impute missing values in a dataset by iteratively estimating each missing value based on the observed data and other parameters in the set. It is a versatile approach as it can handle various types of missing data, making it suitable for situations where the missing values occur randomly [32].

The analysis to set up a predictive model consists of the following steps:

1. Examine the crude univariate relationship between predictors and LOS.
    a. For continuous variables check whether they are normally distributed (= Histogram)
        i. continuous variables: normally distributed = T-test, not normally distributed = Mann-Whitney U-TEST.
    b. For categorical/nominal variables: Chi2-test or Fisher's Exact test.

    c. Calculate Odds Ratios (OR): measure the association between the variable and the outcome of LOS using a cross-tab.
2. Multivariate logistic regression model.
    a. Conduct MICE to complete the missing data.
    b. Test multicollinearity with a correlation test.
    c. Based on the p-values, the odds ratios, correlation tests and the literature a conditional forward stepwise inclusion was applied. The cutoff value for the p-value was set at 0.2.
3. Test the multivariate model.
    a. Test for the most optimal Area Under the Curve (AUC) with significant predictors ($p < 0.1$) [33].
    b. Verify predictor selection against literature.
4. Validation of the logistic regression model.
    a. Model fit; Hosmer-Lemeshow goodness-of-fit.
    b. Validation; K-fold cross-validation & Calibration plot.

3. RESULTS

3.1 DESCRIPTIVE ANALYSIS

Between April 2021 and March 2023, figure 1 shows a schematic overview of the final patient selection. 44 patients did not meet the inclusion criteria, so 210 patients were included in the analysis.

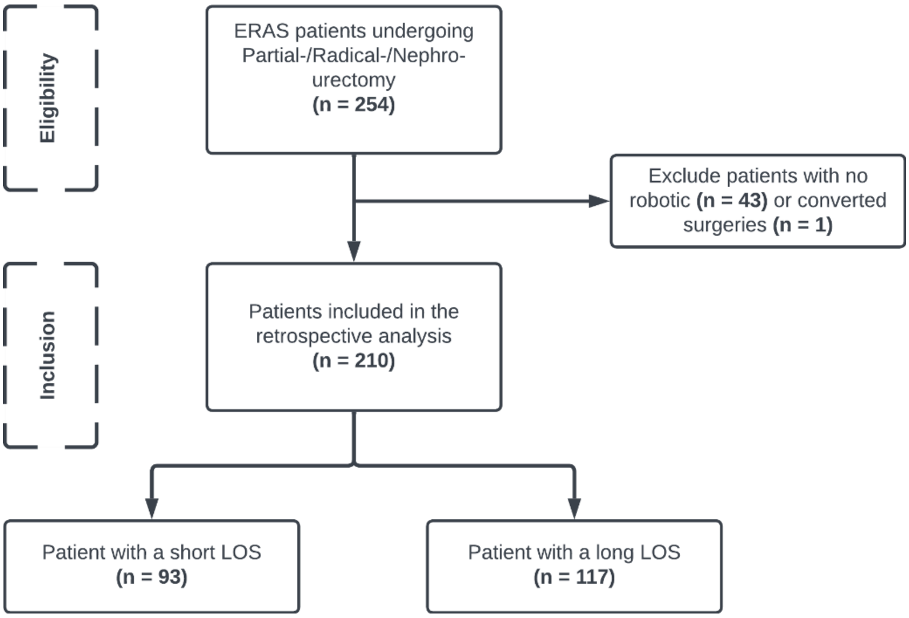

Figure 1: flow diagram to outline the selection process for the study population

Length of stay is summarized as Mean = 1.95 nights, Standard Deviation (SD) = 1.36 nights. As the outcome measure is divided into two categories, the outcomes are as follows: 93 patients with LOS ≤1 night (short) and 117 patients with LOS >1 night (long).

Table 4, 'Characteristics of the ERAS group renal operation,' presents descriptive data for the 210 patients in this study:

Patient Characteristics: The average ages of the patients were 63.5 and 67.3 years old, respectively. Female patients exhibited a 1.74 probability of experiencing a long LOS. While BMI showed no significant association with LOS ($p = 0.68$), pulmonary disease emerged as a notable comorbidity significantly linked to LOS ($p = 0.02$).

Operation Procedure and Lesion-specific Variables: The variables 'Procedure and Lesion size' ($p < 0.001$) and lesion location ($p = 0.06$) demonstrated associations with LOS.

Questionnaire Outcomes: Significant associations were observed between LOS and MET-score ($p = 0.01$) as well as dyspnoea-score ($p = 0.02$).

Lab Values: Several lab values exhibited significant associations with LOS, including haematocrit ($p = 0.004$), haemoglobin ($p = 0.01$), creatinine ($p = 0.03$), and eGFR ($p = 0.02$).

Table 4: Characteristics of the ERAS group renal operations

Characteristics		**Short LOS** (n = 93)	**Long LOS** (n = 117)	**OR for LOS > 1 night**	**p-value** univariate	**p-value** imputations
Patient characterisation						
Age:	*Mean (SD)*	63.5 (10.8)	67.3 (13.5)	1.03	0.03	
Gender:				1.74	0.06	
Females	*N (%)*	30 (32.3)	53 (45.3)			
BMI:					0.68	0.76
Normal	*N (%)*	30 (33)	44 (38.9)	*Ref.*		
Overweight		41 (45)	46 (43.4)	0.77		
Obese		20 (22)	23 (19.7)	0.78		
Missing		*2*	*4*			
Diabetes: Yes	*N (%)*	13 (14)	20 (17.1)	1.27	0.54	
Severe pulmonary disease: Yes	*N (%)*	7 (7.5)	22 (18.8)	2.85	0.02	
Severe heart disease: Yes	*N (%)*	11 (11.8)	15 (12.8)	1.10	0.83	
Alcohol: Yes	*N (%)*	49 (52.7)	50 (42.7)	0.67	0.15	
Smoking: Yes	*N (%)*	29 (31.2)	25 (21.4)	0.60	0.11	
Recreational drug use: Yes[1]	*N (%)*	0 (0)	2 (1.7)	------	0.21	
Operation procedure and lesion-specific variables						
Procedure & Lesion size					<0.001	
Partial & lesion size<4cm	*N (%)*	41(44.1)	21(17.9)	*Ref.*		
Partial & lesion size≥4cm		16(17.2)	12(10.3)	1.46		
Radical & lesion size<9cm		24(25.8)	47(40.2)	3.82		
Radical & lesion size≥9cm		2(2.2)	6(5.1)	5.86		
Nephroureterectomy		10(10.8)	31(26.5)	6.05		
Lesion side:				1.39	0.24	
Right	*N (%)*	44 (47.2)	65 (55.6)			
Lesion location:					0.08	0.06
Upper pole	*N (%)*	31 (33.7)	27 (24.3)	0.54		
Central pole		16 (17.4)	24 (21.6)	0.94		
Lower pole		26 (28.3)	20 (18.1)	0.48		
Overlap		9 (9.8)	24 (21.6)	1.67		
Whole kidney		10 (10.7)	16 (14.4)	*Ref.*		
Missing		*1*	*6*			
Questionnaire outcomes						
SNAQ-score:				1.54	0.20	
Moderate/poor	*N (%)*	17 (18.3)	30 (25.6)			
KATZADL-score:				3.11	0.08	
Dependent	*N (%)*	3 (3.2)	11 (9.4)			
Dyspnoea-score:				1.99	0.02	
Dyspnoea	*N (%)*	28 (30.1)	54 (46.2)			
MET-score:				2.77	0.04	0.01
Poor condition	*N (%)*	6 (7.7)	18 (18.7)			
Missing		*15*	*21*			
ASA physical status:				1.49	0.21	0.16
Group1&2	*N (%)*	61 (66.3)	67 (57.8)			

Group3&4		31 (33.7)	49 (42.2)			
Missing		*1*	*1*			
Lab values						
Haematocrit preoperatively:				2.46	0.02	0.004
Outside normal values	*N (%)*	11 (14.5)	30 (29.4)			
Missing		*17*	*15*			
Haemoglobin preoperatively:					0.02	0.01
Low	*N (%)*	1 (1.2)	4 (3.6)	4.05		
Moderate		13 (15.1)	33 (30)	2.60		
Good		72 (83.7)	73 (66.4)	*Ref.*		
Missing		*7*	*7*			
Creatine preoperatively:	*N (%)*			2.08	0.02	0.03
Too high		24 (27.9)	50 (44.6)			
Missing		*7*	*5*			
eGFR:					0.03	0.03
Poor	*N (%)*	1 (1.2)	12 (10.7)	11.5		
Moderate		11 (12.9)	14 (12.5)	1.02		
Good		73 (85.9)	86 (76.8)	*Ref.*		
Missing		*8*	*5*			

[1]Group is too small to do any calculations

Abbreviations: OR = Odds Ratio, BMI = Body Mass Index, ASA = American Society of Anaesthesiologists, MET = Metabolic Equivalent of Tasks, SNAQ = Short Nutritional Assessment Questionnaire, KATZ-ADL = Katz index of independence in Activities of Daily Living & eGFR = estimated Glomerular Filtration Rate.

Ref.: reference category

3.2 PREDICTIVE VARIABLES

After employing the conditional forward stepwise inclusion method, six variables were selected for inclusion in the multivariate logistic regression analysis. The selection process was guided by the significance levels obtained from Table 5, insights gleaned from relevant literature, correlation tests, and pragmatic considerations in line with established medical knowledge. The model's coefficients, odds ratios, and corresponding p-values are detailed in Table 5.

Table 5: Outcomes Logistic Regression Analysis

Coefficient	**Estimate**	**OR for LOS > 1 night**	**95%CI OR**	**p-value**
Intercept	-1.16			
Partial & lesion size <4cm	*Ref.*			
- Partial & lesion size ≥4cm	0.10	1.11	0.38-3.12	0.85
- Radical & lesion size <9cm	1.51	4.53	2.11-10.13	<0.001
- Radical & lesion size ≥9cm	1.99	7.32	1.43-56.55	0.03
- Nephroureterectomy	1.91	6.72	2.57-18.92	<0.001
Severe pulmonary disease; No	*Ref.*			
- Pulmonary disease; Yes	1.49	4.42	1.63-13.4	0.01
Dyspnoea; No	*Ref.*			
- Dyspnoea; Yes	0.75	2.12	1.10-4.17	0.03
GFR; Good	*Ref.*			
- GFR; Moderate	0.01	1.01	0.41-2.50	0.98
- GFR; Poor	2.06	7.86	1.37-149.50	0.06
Smoker; No	*Ref.*			
- Smoker: Yes	-0.93	0.39	0.18-0.83	0.02
MET-score; Good	*Ref.*			
- MET-score; Poor	0.87	2.38	0.90-6.88	0.09

Ref.: reference category

The multivariate logistic regression analysis identifies several factors associated with prolonged LOS following nephrectomy surgery. Patients undergoing radical nephrectomy, nephroureterectomy, or having larger lesion sizes show increased odds of extended LOS, with ORs ranging from 4.53 to 7.32. Additionally, the presence of severe pulmonary disease and positive dyspnoea-scores are associated with higher odds of prolonged LOS, with ORs of 4.42 and 2.12, respectively. Smokers exhibit lower odds of prolonged LOS (OR: 0.39). Notably, patients with poor Glomerular Filtration Rate (GFR) values have substantially higher odds of extended LOS (OR: 7.86). The association between a poor MET-score and LOS shows a trend towards longer LOS. Among these factors, the parameter contributing the most to the predictive model is radical nephrectomy with lesion sizes ≥9cm, as it demonstrates the highest odds ratio (OR: 7.32) for prolonged LOS.

The Area Under the Curve (AUC), of the logistic regression model yielded an AUC-value of approximately 0.79 (95% CI: 0.72 – 0.85)(see Figure 2).

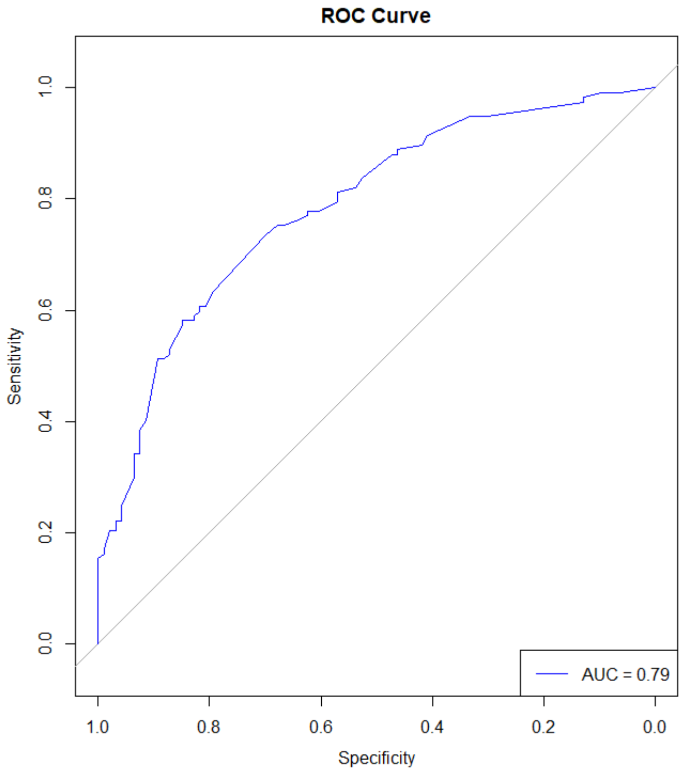

Figure 2: ROC Curve predictive value

3.3 MODEL FIT

The Hosmer-Lemeshow goodness-of-fit test was conducted to assess the fit of the logistic regression model to the data, resulting in a p-value of 0.96. This non-significant p-value suggests that there is no strong evidence to reject the null hypothesis, indicating good fit of the logistic regression model to the data. Therefore, the model adequately predicts LOS following nephrectomy surgery.

3.4 MODEL VALIDATION

The cross-validation results indicate an average accuracy of approximately 67.8% across all folds. Additionally, Cohen's kappa statistic, measuring the agreement between observed and predicted classifications, was found to be approximately 0.34.

The calibration plot (Figure 3) demonstrates the alignment between predicted probabilities and observed outcomes for the logistic regression model. The close proximity of the blue dots to the red line suggests excellent calibration, indicating that the model's predicted probabilities accurately reflect the actual probabilities of the outcomes. This high level of calibration enhances the model's reliability and suitability for practical applications.

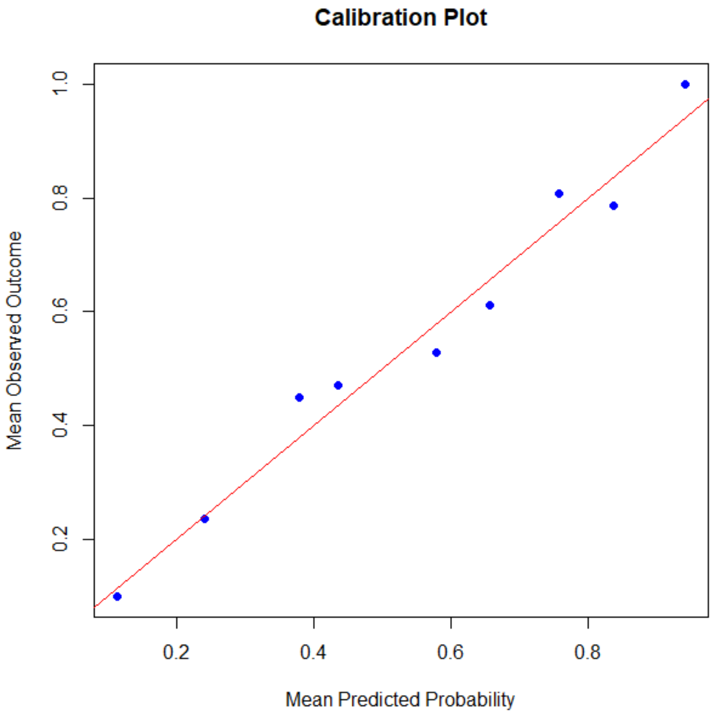

Figure 3: Calibration plot

4. DISCUSSION

The analysis of 210 patients undergoing nephrectomy surgery in the MST within the ERAS program revealed key factors associated with LOS. Resulting in a predictive model including 'Procedure & Lesion size', severe pulmonary disease, dyspnoea, GFR, smoker and MET-score. The logistic regression model demonstrated a good fit to the data, with a Hosmer-Lemeshow p-value of 0.96 indicating no significant evidence to reject the null hypothesis. The model's Area Under the Curve (AUC) value of approximately 0.79 suggests strong discriminatory power, further supported by cross-validation results showing an average accuracy of approximately 67.8% and Cohen's kappa statistic of approximately 0.34. Additionally, the calibration plot demonstrated excellent alignment between predicted probabilities and observed outcomes, enhancing the model's reliability and suitability for predicting LOS following nephrectomy surgery. Overall, the final model provides valuable insights into the factors associated with LOS and demonstrates good predictive performance.

The literature demonstrates that minimally invasive procedures lead to decreased LOS, indicating that partial nephrectomy has a shorter LOS compared to the more invasive radical nephrectomy or nephroureterectomy [34]. Additionally, literature review in the field indicates that the size of the renal lesion plays a significant role in preoperative counselling. Studies suggest that lesion size can impact treatment decisions and outcomes [35]. Making 'Procedure & Lesion size' a critical predictor in the predictive model for LOS.

Several ERAS guidelines already utilize risk stratification models to optimize discharge protocols, with comorbidities playing a key role in negatively impacting patient recovery [23]. Notably, the presence of pulmonary disease significantly increases the risk of prolonged LOS. Previous research has demonstrated the impact of dyspnoea on surgical outcomes. Consistent with these findings, our study reveals a significant association between varying degrees of dyspnoea and prolonged LOS [36]. Both pulmonary diseases and dyspnoea can be included as predictive parameters in a model without correlating strongly due to the multifactorial nature of respiratory health, where dyspnoea may result from various factors beyond the pulmonary diseases like cardiac conditions, anaemia, obesity, or anxiety.

Literature also shows that a lower GFR was associated with a higher risk of a longer LOS after renal surgery [37]. Within this study, this is mainly seen in the group of patients with a GFR score of 'poor', as this group has an odds ratio of 7.85 on a longer LOS compared to the patients with a GFR considered 'good'. The association between a lower MET-score and extended hospital stay after surgery, as indicated in the literature, is corroborated by the results of our multivariate analysis [38]. However MET-score appears uncertain, with an OR of 2.38 and a wide CI of 0.90-6.88.

While smoking is typically associated with negative postoperative outcomes and extended hospital stays in the literature, our study yielded a surprising result: smokers demonstrated a significantly reduced likelihood of prolonged LOS [39][40]. However, it is essential to approach this finding with caution and consider several factors. Firstly, the concept of recovery may differ from the duration of LOS, and early discharge does not necessarily indicate complete recovery. In the literature, smoking is also a significant predictor of readmissions and reoperations in patients undergoing surgery [41]. However, in this study, these outcome measures have been omitted. Additionally, discussions with experts suggest that patients who smoke may express a greater motivation to return home, possibly influenced by their desire to resume smoking. This interpretation contrasts with existing literature, which predominantly links smoking with longer hospital stays [42]. Currently lifetime exposure to smoking is considered as more influential on complications and LOS than current smoking status, which can be a possible explanation for this discrepancy for smokers in this study [43].

The significant association between haemoglobin and LOS observed in the univariate analysis aligns with the literature. Although haemoglobin was initially identified as a predictive variable for LOS in this study, it was not retained in the final multivariate analysis. Nonetheless, the initial findings underscore the potential importance of preoperative haemoglobin levels in predicting LOS following nephrectomy within the ERAS framework. The classification of postoperative anaemia by the World Health Organization continues to offer valuable insights for preoperative treatments, with the potential to enhance recovery rates and reduce hospital stays [44]. Similarly, the literature highlights the potential significance of additional laboratory values, such as preoperative haematocrit, in predicting LOS. Lorentz (2015) demonstrated the impact of preoperative haematocrit on LOS for patients undergoing nephrectomy [45]. While creatinine was considered for inclusion in the model, it did not demonstrate a significant effect on the predictive capability of the model, despite its potential importance in predicting surgical outcomes and postoperative survival for cancer patients [46]. The absence of creatinine in the logistic regression can be explained by its strong correlation to the variable GFR, which was included.

The shortcoming of this study was the absence of the preoperative albumin value in this study. A study from Lorentz (2015) showed that albumin holds great predictive values in a linear regression model for LOS [45]. Due to over 60% missing albumin data in the 210 observations of this study, albumin could not be included in the analysis. This missing data is attributed to selective puncturing, where values of those referred or patients with mild cancers were missing. Additionally, albumin was deemed ineligible for MICE implementation, as it exceeded the 50% cut-off value for inclusion in the imputation process. A side note to mention is that albumin, besides other functions, serves as an indicator of renal failure. However, in this study, renal function is primarily assessed using creatinine or eGFR. Other variables with potentially predictive values missing include the R.E.N.A.L.-score (radius, exophytic/endophytic properties, nearness of tumour to collecting system or sinus, anterior/posterior, hilar tumour touching the main renal artery or vein and location relative to polar lines) or the PADUA-score (preoperative aspects and dimensions used for an anatomical) [47]. These systems measure the complexity of the tumour/lesion but were not measured. Both are very similar and can help to be guide in nephron-sparing surgeries, however the predictive value of these guides can be questioned as tumour complexity only partially explain prolonged LOS [48][49]. Another shortcoming can be the pivotal role of attitude and home situation in determining a patient's discharge readiness. Variables related to the patients attitude or home situations which can be measured in a follow-up study are: motivation for recovery, marital status, availability of home care, presence of familial caregivers, and living arrangements.

The completion of missing data using the MICE function RStudio could have some influence on the model. Firstly, imputing missing data introduces uncertainty into the dataset, which may affect the precision of estimates and increase variability in the results. Secondly, the imputation process relies on assumptions about the missing data mechanism, and any violations of these assumptions could introduce bias into the analysis. Additionally, imputed values may not accurately represent the true values of the missing data, potentially leading to misclassification or distortion of relationships between variables. Therefore, careful consideration of the imputation process and its potential effects on the study outcomes is crucial for interpreting the results accurately.

It is important to recognize the inherent limitations in the external validation of predictive models. A validation study conducted in one place at one time with a specific group of patients is like a single time frame. It gives us a good idea of how well the prediction model works in that exact situation, but we can not be sure it will work the same way in different places or time frames [50]. Inclusion of multiple settings/locations when developing a predictive model or using the appropriate statistical methodology could be recommended for external validation. In terms of internal validation, the dataset utilized in this study encompasses information up to March 2023, presenting an opportunity to internally validate the model using data collected beyond this period. Consider to monitor the performance of the predictive model overtime and update the model when necessary, thereby enhancing the reliability of the findings.

Recommendations for follow-up studies based on the findings of this research can help further enhance our understanding of the factors associated with LOS and patient outcomes in renal surgery. Firstly, considering the choice of regression model and a dichotomous outcome measure, future studies with larger populations could explore the use of linear regression to accommodate increased variance in LOS, thereby allowing for more precise predictions. Which was not possible in this study due to the lack of variability in LOS. Additionally, expanding the scope of the investigation beyond LOS to include postoperative complications and readmissions as outcomes would provide valuable insights into the broader spectrum of patient recovery and healthcare utilization. Moreover, given that the impact of patient attitudes and coping mechanisms on LOS was mentioned by several experts, follow-up studies could incorporate assessments of patient attitudes and coping strategies, as well as explore aspects of the home environment and available help from relatives. Collectively, these recommendations aim to contribute to a more comprehensive understanding of the factors influencing patient outcomes in renal surgery and inform strategies for optimizing patient care and recovery.

The developed model offers valuable informative insights into a patients LOS following radical partial nephrectomy or nephroureterectomy, which can be communicated to patients during consultations with urologists. The informative nature of the predictive model can empowers patients to prepare for their postoperative recovery, whether by arranging home accommodations or anticipating potential longer LOS. For the healthcare professionals this tool can help to identify patient-specific risk factors and can help tailor care plans. For example the literature shows that pulmonary rehabilitation may help reduce postoperative outcomes within the ERAS program [51]. Doctors may initiate this rehabilitation before patients undergo surgery. Similarly, patients can improve their condition by training their MET-score during the waiting period, which could lead to better postoperative outcomes. Doctors must emphasize to patients the significance of shorter hospital stays equating to better recovery. It is crucial for patients to understand that prolonged hospitalization increases the risk of Hospital Acquired Infection, institutionalization, and deconditioning, leading to loss of physical and cognitive capabilities. Additionally, the determinations about LOS can inform hospital policies and operational planning surrounding surgeries. For instance, planners can consider patients with expected longer LOS when allocating department rooms. This information is particularly valuable given the existing high demand for hospital beds. To effectively implement the findings of this study at MST, several essential steps must be undertaken. Validation of the model and compliance with regulatory standards, such as the Medical Device Regulation (MDR), must be done first. Particularly, considerations for classification as a communicative device or medical device under the MDR framework must be addressed. Ultimately, the deployment of visualizations tailored to patient communication via platforms like PowerBi represents a promising avenue for enhancing patient understanding and engagement in their care journey.

5. CONCLUSION

In conclusion, this study addresses the knowledge gap in defining the predictive variables associated with the LOS for renal patients within the ERAS program in the MST. Through an analysis of patient data, including patient characteristics, operation and lesion-specific variables, questionnaires and lab values, valuable insights have been gained into the determinants of LOS in this patient population. The clinical implementation of these findings can be used by patients, doctors, planners or policymakers. Examples of these implementations are guiding patient expectations and informing, personal advice for better recovery and prehabilitation or hospital planning. For instance, initiating pulmonary rehabilitation or focusing on improving MET-score during the preoperative period may lead to a shorter LOS. The doctors play a crucial role in informing patients about the benefits of recovering at home, which is associated with shorter LOS and improved post-surgery recovery.

In essence, this study contributes valuable insights into the preoperative variables associated to LOS after nephrectomy surgery, laying the groundwork for future research and improvements in patient care. Ultimately, both the hospital and the patient should aim for a short LOS after nephrectomies in MST for patients within the ERAS program. This is because patients tend to recover more successfully at home, while hospitals can alleviate the burden on healthcare resources, especially during periods of high demand.

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