SAFE DISCHARGE

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RESEARCH QUESTION

"To what extent are health status factors during hospital stay predictors for safe discharge after esophagectomy in esophageal cancer patients?"

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Abstract

Background: The main curative treatment for patients with esophageal cancer is esophagectomy. Currently, the median perioperative hospital stay after esophagectomy is twelve days in the Netherlands. Fast track surgery (FTS) focusses on optimizing perioperative care, with the aim to enhance recovery, reduce morbidity and mortality rates, and decrease the length of hospital stay after major surgery. Implementing the FTS protocol should be done with high regard for safety, preferably based on factors predicting safe discharge.

Objective. Identifying predictors during hospital stay for safe discharge after esophagectomy in esophageal cancer patients.

Design. Quantitative retrospective.

Population. The study population contains esophageal cancer patients who underwent an esophagectomy in the Ziekenhuisgroep Twente (ZGT) Almelo from November 2013 to March 2017.

Method. Data is extracted from the Dutch Upper GI Cancer Audit (DUCA) database, databases composed for former research within the ZGT, and in the Electronic Patient Record (EPR) from 124 patients. To combine the data an Access form was developed. After data input, data was analyzed by SPSS Statistics 24. First, univariate analyses were performed, followed by a logistic regression.

Results. Logistic regression showed significant differences between groups based on body temperature on day three, heart rate on day thirteen and a lower blood pressure from day eleven to twelve.

Conclusion. Three health status factors have shown significant association with safe discharge. These are a lower body temperature on day three, a lower heart rate on day thirteen, and a drop in lower blood pressure from day eleven to day twelve.

Introduction

In the Netherlands, esophageal and cardia cancer are listed as the eighth most common cancer encountered among men, with a percentage of 3.7 (1). In 2016, the prevalence of esophageal cancer was 5234 in the Netherlands (2). The diagnosis esophageal cancer was given 2545 times, from which 72 percent were men (3). Being diagnosed with esophageal cancer leads to death within five years for 81 percent of the patients in the Netherlands (4).

Treatments of cancer can either have a curative or palliative focus. In sixty to seventy percent of the esophageal cancer cases, distant metastases are already present by the time symptoms and signs appear, which means palliative treatment is the only option left (5,6). There are three types of treatment possible at this stage: radiotherapy, endoprothesis placement and chemotherapy. All three options focus on suppressing the tumor growth and alleviation of complaints.

In case the tumor and metastases are of limited size, curative treatment is often possible (5). The main curative treatment for patients with esophageal cancer is esophagectomy (6). At this surgery, the part of the esophagus where the tumor is located is removed. After this, the remaining parts of the esophagus or stomach are connected. There are two ways to do this, by intrathoracic anastomosis (Ivor-Lewis) or

cervical anastomosis (McKeown) (7). Esophagectomy is often executed in combination with chemoradiotherapy to increase the probability of success (5,6).

Currently, the median perioperative hospital stay after esophagectomy is twelve days in the Netherlands (8). Fast track surgery (FTS) focusses on optimizing perioperative care (9,10), with the aim to enhance recovery, reduce morbidity and mortality rates, and decrease the length of hospital stay after major surgery (11). Previously conducted research has shown that the average length of hospital stay can be reduced from twelve to eight days by implementing the fast track surgery protocol (12).

In order to support the safety of the fast track protocol, safe discharge criteria are important. Using these criteria aims to prevent complications caused by too early discharge. There is no information available for discharge criteria after esophagectomy in the national guideline (13). It remains, therefore, unclear at which admission day and under which health circumstances the discharge after esophagectomy is safe and the most optimal. This research contributed to determining safe discharge criteria for the fast track protocol, by identifying which health status factors are predictors for safe discharge. When referring to "health status", the following definition will be used: "Level of health of an individual person, a group, or a population as assessed by that individual or by objective measures" (14). These health status factors in this research are among others patient's body temperature, blood pressure, and mobility. Former research has showed that postoperative complications are associated with a high American Society of Anaesthesiology (ASA) rating, presence of comorbidity, old age (over 75 years old), black race, congestive heart failure, coronary artery disease, peripheral vascular disease, hypertension, insulin-dependent diabetes, smoking status, and steroid use (8,15). The ASA rate is a way to classify the physical status of the patient. An ASA rate of I is attributed to a normal healthy patient, while an ASA rate of VI is attributed to a declared brain-dead patient (16). The ASA rate per stage is outlined in Appendix 3.

The research question examined during this research is as follows: "To what extent are health status factors during hospital stay predictors for safe discharge after esophagectomy in esophageal cancer patients?"

Patients and methods

The research was conducted at the surgery department in the ZGT Almelo. The ZGT is planning on implementing a fast track protocol for patients who underwent esophagectomy. The study population contains patients who underwent an esophagectomy in the ZGT Almelo from November 2013 to March 2017. Patients who died in hospital before discharge are excluded from the analyses.

The research conducted was a quantitative retrospective research, which means previously collected data was used. This data was documented within the Dutch Upper GI Cancer Audit (DUCA) database, databases composed for former research within the ZGT, and in the Electronic Patient Record (EPR), in several documentation manners. Therefore, it was essential the required data was processed into the same format. In order to combine data from both existing databases and the EPR, an Access form was developed and used. This form consisted patient's information divided into standard parameters, daily parameters, readmissions, and complications. The daily parameters are documented from the day of surgery

(day 0) to the day of discharge. In case a patient was in the hospital for more than fourteen days, daily parameters were documented until day fourteen. The discharge date was noted so that the total amount of days spent in the hospital could be calculated. Besides that, patients who were in the hospital for more than 14 days were not included in the analyses concerning the last day of hospital stay. An overview of all the variables and their documentation can be found in Appendix 2.

Outcome measures

Safe discharge was determined based on readmission or death within thirty days after discharge. Safe discharge covers patients without any readmission as well as patients who were readmitted with a Clavien-Dindo classification of I or II. Readmission classified with a Clavien-Dindo of III or higher, including death of the patient, was determined as unsafe discharge.

The documented variables can be separated into baseline characteristics, daily parameters, and readmission data. Examples of baseline characteristics are gender, body mass index (BMI), age, operation date and ASA score. Daily parameters documented are among others body temperature, heart rate, and blood values such as leucocytes and C-reactive protein (CRP). The readmission data contains for example information about the date of readmission, its reason and the corresponding Clavien-Dindo score. A total overview of all variables and their documentation manners is shown in Appendix 2.

In addition to these variables, new variables were created. From all patients who were in the hospital for a maximum of fourteen days after surgery, the last day was identified and variables were analyzed. The same was done for the day before discharge, two days before discharge and three days before discharge. Besides that, new variables were created to be able to analyze the influence of daily variation. The rise or drop of all continuous variables was identified by creating a variable showing this variation. For example, the body temperature on day three was subtracted from the body temperature on day four and formed into a new variable. The same was done to identify the variation between the last day of hospital stay and the first day after surgery. For example, the heart rate on day one was subtracted from the heart rate on the last day of hospital stay. Last variables created concerned the variation between the day before discharge and the first day after surgery. For example, the upper blood pressure on day one was subtracted from the upper blood pressure on the day before discharge.

In order to answer the research question, several analyses are conducted. First, it was important to gain insight into the average length of hospital stay in the current situation. Second, gaining insight into the percentage of patients readmitted within thirty days after discharge was relevant to support the outcomes. It was also relevant to know the percentage of patients who died within thirty days after discharge. This information could be used to split the population into the safe and unsafe discharge groups. In addition, an overview of the reasons for these readmissions and deaths had to be made. Combining results from these analyses could lead to an overview of health status factors associated with safe discharge.

Important to mention is the parallel study called Nutrient. The patients participating in this study started oral intake directly following esophagectomy. This contrasts with the conventional protocol in which patients receive jejunostomy feeding for the first five postoperative days, and are not allowed to take any oral feeding. The aim of the nutrient study is to determine the feasibility and safety of early oral intake

(17). The first nutrient study only contained patients who started oral intake directly following esophagectomy. However, the follow-up study, called Nutrient 2, contains patients within the early nutrition group as well as a group of patients following the conventional protocol.

The p-value used to determine significance is five percent. All variables which showed a two-tailed significance or two-sided asymptotic significance level of five percent or lower were considered as variant between the safe and unsafe discharge group.

Statistical analysis

The study population was divided into two groups, a group which was discharged safely and a group which was not. During the research, data collected from DUCA and the EPR was analyzed to identify which variables are associated with safe discharge. Data was analyzed using SPSS (Statistics 24), comparing two unpaired groups.

First, univariate tests were conducted to determine which variables are associated with safe discharge. Categorical variables were analyzed using the Chi-square test. These variables were gender, ASA score, comorbidity, surgery type, nutrient study participation, malaise, diuretic, mobility, and pain score. Continuous variables with a normal distribution were analyzed using the Student T-test. Normally distributed variables were age, BMI, body temperature, upper blood pressure, lower blood pressure and the leucocytes level. Not normal distributed continuous variables were analyzed using a Mann-Whitney U test. These variables were the length of hospital stay, weight loss, the number of days in intensive care, heart rate, respiratory rate, C-reactive protein (CRP) level and amylase level. In order to determine which variables needed to be included in the logistic regression, a significance level of five percent was used.

Second, a logistic regression (forward selection) was conducted on the variables with a significant difference within the univariate analyses, to determine the strength of association with safe discharge of these variables. During logistic regression, a significance level of five percent was used.

Results

The characteristics of the 124 patients are summarized in Table 1. The safe discharge group contained 109 patients, against 15 patients within the unsafe discharge group. Since there was only one patient with an American Society of Anaesthesiologists (ASA) score of four, thus the ASA scores three and four are combined for data analyses. As can be seen, there are significant differences between the safe and unsafe discharge groups based on ASA score, year of surgery, complications (at least one), complications during primary hospital stay and readmissions. The p-value of 0.04 concerning the ASA score shows there is a significant difference between categories. Similar to this, the year of surgery shows a significant influence, with a p-value of 0.02. However, the exact location of these differences is unknown. The number of complications was significantly lower in the safe discharge group, with a p-value of 0.02. In addition, the number of patients with a complication during primary hospital stay is significantly lower within the safe discharge group, with a p-value of 0.00. The safe discharge group contained fewer patients who were readmitted, with a p-value of 0.00. All other baseline variables did not show any significant differences between groups.

Within the Nutrient study, the early (21 patients (77.8%)) versus delayed (6 patients (22.2%)) nutrition analysis was made because the patients in the first Nutrient study followed the same nutrition protocol as part of the patients in the Nutrient 2 study (17). The other part of the patients in the Nutrient 2 study received nutrition following the conventional, delayed nutrition protocol. However, no significant differences (Pearson Chi-Square: 0.62) were found between the early and delayed nutrition groups. Within the early nutrition group, 19 patients (90.5%) were discharged safely. Within the delayed nutrition group, 5 patients were discharged safely (83.3%).

Table 1: Baseline characteristics

Esophageal cancer			**Safe discharge (n=109)**	**Unsafe discharge (n=15)**	**p-value***
Gender	*Male*	n (%)	89 (88.1)	12 (11.9)	0.88[1]
	Female	n (%)	20 (87.0)	3 (13.0)	
Age		Mean (SD)	65.12 (8.59)	64.00 (10.26)	0.65[2]
	Male	Mean (SD)	64.96 (9.06)	64.67 (10.80)	0.92[2]
	Female	Mean (SD)	65.85 (6.23)	61.33 (9.07)	0.28[2]
ASA**		Count			0.04[1]
	1	n (%)	17 (15.6)	2 (13.3)	
	2	n (%)	65 (59.6)	7 (46.7)	
	3	n (%)	27 (24.8)	5 (33.3)	
	4	n (%)	0	1 (6.7)	
Comorbidity (1 or more)		n (%)	85 (78.0)	11 (73.3)	0.69[1]
	Cardiac	n (%)	4 (4.7)	2 (18.2)	
	Vascular	n (%)	48 (56.5)	7 (63.6)	
	Diabetes	n (%)	18 (21.2)	4 (36.4)	
	Pulmonic	n (%)	27 (31.8)	4 (36.4)	
	Neurologic/psychiatric	n (%)	17 (20.0)	3 (27.3)	
	Stomach/intestine	n (%)	21 (24.7)	5 (45.5)	
	Urogenital	n (%)	7 (8.2)	0	
	Thrombotic	n (%)	4 (4.7)	2 (18.2)	
	Neuromuscular	n (%)	12 (14.1)	5 (45.5)	
	Endocrine disorders	n (%)	6 (7.1)	1 (9.1)	
	Infectious diseases	n (%)	2 (2.4)	0	
	Other	n (%)	30 (35.3)	1 (9.1)	
BMI***		Mean (SD)	26.45 (4.36)	26.48 (3.53)	0.98[2]
Weight loss		Median (IQR)	3.00 (0 – 7.0)	5.00 (0 – 10.75)	0.37[3]
Year of surgery		Count			0.02[1]
	2013	n (%)	4 (100)	0 (0)	
	2014	n (%)	39 (88.6)	5 (11.4)	
	2015	n (%)	24 (88.9)	3 (11.1)	
	2016	n (%)	38 (92.7)	3 (7.3)	
	2017	n (%)	4 (50)	4 (50)	
Surgery type		Count			0.08[1]
	Ivor Lewis	n (%)	94 (86.2)	14 (93.3)	
	McKeown	n (%)	14 (12.8)	0 (0)	
	Other	n (%)	1 (0.9)	1 (6.7)	
Nutrient study		Count			0.25[1]

1 – early nutrition	n (%)	12 (11.0)	0	
2 – early nutrition	n (%)	7 (6.4)	2 (13.3)	
2 – delayed nutrition	n (%)	5 (4.6)	1 (6.7)	
Days on intensive care	Median (IQR)	1 (1 – 3)	1 (1 – 3)	0.41[3]
Hospital stay (in days)	Median (IQR)	11 (9 - 19)	11 (8 - 24)	0.91[3]
Complication (1 or more)	n (%)	67 (61.5)	14 (93.3)	0.02[1]
Complication (1 or more) during primary hospital stay	n (%)	13 (24.5)	6 (85.7)	0.00[1]
Readmission	n (%)	11 (10.1)	15 (100)	0.00[1]
Readmission due to complication****	n (%)	7 (70.0)	14 (93.3)	0.12[1]
Grade I	n	7	0	
Grade II	n	2	0	
Grade III	n	2	10	
Grade IV	n	0	4	
Grade V	n	0	1	
Readmission day (after discharge)	Median (IQR)	7 (4 – 65)	5 (2 – 15)	0.24[3]
Readmission within 30 days	n (%)	8 (7.3)	15 (100)	0.03[1]
Mortality	n (%)	24 (22.0)	2 (13.3)	0.35[1]
30 days' mortality (after discharge)	n (%)	0	1 (6.7)	

* Performed analyses differed, depending on categorical/continuous variables and the distribution.

[1] Chi-square test was performed, asymptotic significance (2-sided) of the Pearson Chi-Square is shown.

[2] Student T-test was performed, significance (2-tailed) is shown.

[3] Mann-Whitney U test was performed, asymptotic significance (2-sided) is shown.

** American Society of Anaesthesiologists score

*** Body Mass Index

**** Readmission at any time, not limited to the thirty days after discharge

After analyzing the baseline characteristics of both groups, univariate analyses were performed to assess the influence of health status factors on the dependent variable safe discharge. All variables were tested on a relation between the variable and safe discharge. Categorical variables were tested by a Chi-square test, normally distributed continuous variables by a Student T-Test and not normally distributed continuous variables by a Mann-Whitney U test. In Table 2, only variables which showed a significant difference between the safe and unsafe discharge group are noted. From those variables, either a mean and standard deviation, a median and an interquartile range (IQR) or count and percentage are shown. In addition, the significance level is noted for all variables.

Besides that, all continuous variables were analyzed by differences per day. For example, the variation of body temperature from day one to day two. Significant differences or variables with a borderline significance that were found are shown in Table 2.

In addition, all variables of the last day were analyzed, but no significant differences were found. The same was done for the day before discharge, two days before discharge and three days before discharge. Only when analyzing three days before discharge, a significant difference was found between groups, on the level of leucocytes.

Table 2: Univariate analyses

Variable		**Safe discharge** *Mean/median/count*	**Unsafe discharge** *Mean/median/count*	**p-value* < 0.05**
ASA-score**	Median (IQR)	2 (2 – 2.5) (n=109)	2 (2 – 3) (n=15)	0.04[1]
Body temperature				
Day 3	Mean (SD)	37.6 (0.52) (n=108)	38.1 (0.56) (n=14)	0.00[2]
Day 13	Mean (SD)	37.4 (0.76) (n=42)	38.0 (0.93) (n=7)	0.06[2]
Day 8 – 7	Mean difference (SD)	0.00 (0.58) (n=102)	-0.34 (0.74) (n=14)	0.05[2]
Heart rate				
Day 13	Median (IQR)	91 (85 – 97.25) (n=38)	104 (97 – 110) (n=7)	0.00[3]
Day 14	Median (IQR)	94 (86 – 100) (n=35)	106.5 (99.25 – 113) (n=6)	0.03[3]
Respiratory rate				
Day 1	Median (IQR)	21 (19 – 24) (n=90)	24 (22.5 - 27) (n=13)	0.05[3]
Day 9	Median (IQR)	28 (24.5 – 31.75) (n=16)	22 (n=3)	0.06[3]
Day 12	Median (IQR)	29 (25 – 34) (n=11)	20 (n=2)	0.05[3]
Day 13	Median (IQR)	31 (30 - 35) (n=7)	Not available (n=1)	0.04[3]
Upper blood pressure				
Day 12	Mean (SD)	131.5 (20.73) (n=46)	148.3 (14.63) (n=7)	0.05[2]
Lower blood pressure				
Day 12 – 11	Mean difference (SD)	-1.97 (8.13) (n=31)	12.20 (11.90) (n=5)	0.00[2]
Leucocytes				
Day 9 – 8	Mean difference (SD)	-0.01 (2.52) (n=50)	3.70 (1.22) (n=3)	0.02[2]
3 days before discharge	Mean (SD)	8.19 (2.30) (n=45)	5.47 (2.55) (n=3)	0.05[2]
CRP***				
Day 9	Median (IQR)	107 (54 – 165) (n=67)	230.5 (109.5 – 294.5) (n=4)	0.06[3]
Day 11	Median (IQR)	130 (50 – 181) (n=45)	266 (203.8 – 328.3) (n=4)	0.01[3]
Day 14	Median (IQR)	93 (60 – 136) (n=31)	190 (169 – 232.5) (n=5)	0.00[3]
Amylase				
Day 4 – 3	Median difference (IQR)	-5 (-10 – 1) (n=97)	-3 (-4 – 15) (n=15)	0.06[3]
Day 9 – 8	Median difference (IQR)	0 (-2 – 2) (n=44)	7 (3 - 787) (n=5)	0.02[3]
Pain score				
Day 1	Median (IQR)	0 (0 – 3) (n=79)	2 (0 – 5) (n=13)	0.05[3]
Day 13	Median (IQR)	0 (0 – 0) (n=84)	0 (0 – 1) (n=9)	0.03[3]
Day 14	Median (IQR)	0 (0 – 0) (n=83)	0 (0 – 1.25) (n=10)	0.02[3]

* Performed analyses differed, depending on categorical/continuous variables and the distribution.

[1] Chi-square test was performed, asymptotic significance (2-sided) of the Pearson Chi-Square is shown.

[2] Student T-test was performed, significance (2-tailed) is shown.

[3] Mann-Whitney U test was performed, asymptotic significance (2-sided) is shown.

** American Society of Anaesthesiologists score

*** C-reactive protein

First, results of univariate analyses were scanned on striking results. It is important to point out that some populations are very small. Therefore, it is chosen to exclude variables wherein one of the groups contain less than five patients.

Second, remaining variables with a significant difference within the univariate analyses were tested for correlation within that day. The only variables that showed a significant correlation were body

temperature and heart rate on day thirteen. A significant correlation of 0,332 was found between body temperature and heart rate. Since this correlation is small, it was decided that the variables were fit to analyze them within the same logistic regression model.

Third, logistic regression (forward selection) was conducted per day, containing the significant variables of that day. Table 3 shows the significance level, odds ratio (OR), and Nagelkerke R Square (R^2). The odds ratio is the exponential function of the regression coefficient associated with a one-unit increase in the exposure (18). The R^2 shows the proportion of variance in the dependent variable associated with the predictor (independent) variables (19). The higher the percentage, the stronger the prediction.

There were no significant variables found within the univariate analyses on day two, neither on day four to eleven. The logistic regression conducted for day one contained the variables respiratory rate and pain score. These variables did not show a significant influence on safe discharge. The only variable that showed a significant difference within the univariate analyses on day three was body temperature. The logistic regression model showed that the R^2 of this variable is 12.8%. Similar to day three, the logistic regression for day twelve contained one variable, upper blood pressure. The R^2 of this variable is 67.8%. Day thirteen showed three variables suitable for logistic regression: body temperature, heart rate, and pain score. The model with the highest R^2 contained only heart rate, with a percentage of 40.3. The logistic regression conducted for day fourteen contained heart rate, CRP level, and pain score. No significant influence was found for these variables.

Furthermore, the daily variation showed significant differences in the univariate analyses from day seven to eight, and day eleven to twelve. The variation between day seven and eight showed a borderline significant p-value on body temperature. Lower blood pressure was identified as significant for the variation between day eleven and twelve. The R^2 showed within this analysis was 40.3%.

Table 3: Logistic regression

Variable	**Significance**	**Odds ratio**	**R^2 (%)***
Day 3			12.8
Body temperature	0.01	0.21	
Day 13			67.8
Heart rate	0.04	0.71	
Day 12-11			40.3
Lower blood pressure	0.02	0.85	

* Nagelkerke R Square

According to the results shown in Table 3, predictors are found on day three, day thirteen and the variation from day eleven to twelve. Comparing these results to the outcomes in Table 2, it can be stated that a lower body temperature on day three is associated with safe discharge. In addition, a lower heart rate on day thirteen is associated with safe discharge. Last, analyses showed that a drop in lower blood pressure from day eleven to day twelve is associated with safe discharge.

Discussion

Analyses showed three predicting health status factors for safe discharge, body temperature on day three, heart rate on day thirteen and the drop of lower blood pressure from day eleven to day twelve. For both

body temperature and heart rate applies that a lower value is associated with safe discharge. In case of lower blood pressure, a decrease is associated with safe discharge.

This research contained 124 esophageal cancer patients, all treated with esophagectomy within the ZGT Almelo. We assume that this group is representative of all the esophageal cancer patients treated with esophagectomy within the ZGT Almelo. However, its external validity is limited, because the gender distribution differs. Nationwide, 72 percent of the esophageal cancer patients are men, which is in contrast to the 81 percent of the database composed within this research (3). The mean age is approximately the same (20). Nevertheless, we expect that further research containing more patients will increase internal as well as external validity. In addition, it is expected that analyzing a larger group of patients will identify more predictors, with higher significance levels.

It is remarkable that the predicting factors differ per day; no variable is significant in more than one day according to the logistic regression. A possible explanation for this is the low number of patients. Strikingly, the median hospital stay was eleven days in both groups, which means the significant differences showed within the analyses of day thirteen and day eleven to twelve contained only patients who were in the hospital longer than the median. The exact meaning of these results should be explored in further research. In addition, analyses supported the expectations concerning the influence of the ASA score. Earlier conducted research showed that a higher ASA score is associated with postoperative complications (8,15). Our research showed a similar influence of ASA score on safe discharge.

One interesting finding is that no significant differences were found between groups concerning the last day of hospital stay. Neither did the day before discharge or the day before that day show any significant differences. It could thus be suggested that all patients could have been discharged two days earlier. Another important finding was that the variation between day one and the last day also did not show significant differences between groups. Furthermore, the variation between day one and the day before discharge did not show any significant difference.

Another striking outcome is that the percentage of mortality is higher within the safe discharge group (22 vs. 13.3 percent). However, the cause of death is often not related to the esophagectomy, and the thirty days' mortality is much lower (0 vs. 6.7 percent). Besides that, the average age of women is lower within the unsafe discharge group. These differences are not significant but should be paid attention to in further research.

A possible influential factor is the prospect of the FTS at the end of 2016 and the start of 2017. The FTS protocol was not put in place, but the surgeons were aware of the FTS protocol. Therefore, this might have shortened the length of patients' hospital stay. The median hospital stay within the ZGT is eleven days, which is one day shorter than the national median hospital stay (8). A significant influence of year of surgery was found on safe discharge, with a p-value of 0.02. However, this might be caused by the small number of patients included for 2017. The exact location of this significant difference is unknown. Besides that, the nutrient study possibly affected the outcomes. In this study, the oral intake of food was stimulated and this early oral intake may have influenced both complications and length of hospital stay (17). In addition, the surgery type can be a possible influencing variable. Former research showed advantages in

perioperative outcomes for the Ivor-Lewis anastomosis, compared to the McKeown anastomosis (7). The p-value showed within this research is 0.079, which is borderline significant. However, it is unknown where this difference takes place exactly, and which operation type is safer.

There have been several limitations concerning the outcomes of the study. First, the study population was relatively small. The unsafe discharge group contained fifteen patients, which induced that some analyses could not be conducted, and may have caused lower significance levels. Therefore, no reliable statements could be made, for example, about the influence of respiratory rate on day nine and CRP level on day eleven. The decision was made to exclude the variables with less than five patients in one of the groups, to protect validity and reliability. Nevertheless, these variables can be relevant for further research.

An important recommendation for further research is to increase the number of patients in the analyses. This may increase the number of variables with a significant difference, and therefore, may increase the fit for use of the results. When more variables are found, it is possible to imply those into an applicable prediction model. This model can be used to support the surgeon determining discharge.

Besides that, specifying the complications more on the type and occurring date might give a better insight into safe discharge. By doing this, a better overview can be made which shows the percentage of discharge with already recognized complications versus the unexpected complications. In addition, analyses can be conducted in which a group without complications during hospital stay can be compared to a group with complications during hospital stay. By doing this, predictors for complications, in general, can be provided.

Conclusion

The research question examined during this study is: “To what extent are health status factors during hospital stay predictors for safe discharge after esophagectomy in esophageal cancer patients?”

It can be concluded that the health status factors body temperature on day three, heart rate on day thirteen and the drop of lower blood pressure from day eleven to day twelve are associated with safe discharge. For both body temperature and heart rate applies that a lower value is desirable, concerning safe discharge.

Appendix 1: References

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Appendix 2: Codebook variables Access form

Algemeen

- 0 = nee
- 1 = ja
- 999 = onbekend

Standaard parameters

Table 3: Baseline characteristics

Beschrijving	Veldnaam	Gegevenstype	Codering
Patiënt nummer ZGT	PatNr	Numeriek	
Onderzoeksnummer	ID_onderzoek	Numeriek	
Geboortedatum patiënt	Geboortedatum	Datum/tijd	
Geslacht patiënt	Geslacht	Numeriek	0=man, 1=vrouw
ASA score (1 tot en met 6)	ASA	Numeriek	1-6, waarvan 1=gezond, 6=doodziek
Comorbiditeit (maximaal 6 comorbiditeiten op te geven)	Comorbiditeit	Numeriek	0=geen comorbiditeit, 1=cardiaal, 2=vasculair, 3=diabetes, 4=pulmonaal, 5=neurologisch/psychiatrisch, 6= maag-darm, 7=urogenitaal, 8=trombotisch/stollingsziekten, 9=neuromusculair, 10=endocriene aandoeningen, 11=infectieziekten, 12=overig
Lengte van de patiënt in centimeter	Lengte	Numeriek	
Gewicht van de patiënt preoperatief in kg	Gewicht	Numeriek	
Gewichtsverlies van de patiënt in kg	Gewichtsverlies	Numeriek	
Type tumor	Pathologie	Numeriek	0=adenocarcinoom, 1=plaveisel, 2=adenosquameus
Neoadjuvante therapie type	Neoadj_tx	Numeriek	0=geen neoadjuvante therapie, 1=Chemotherapie, 2=Chemoradiotherapie , 3=Radiotherapie
Operatiedatum	Op_datum	Datum/tijd	
Operatie type	Op_type	Numeriek	0=Ivor Lewis, 1=McKeon, 2=Anders
Deelname Nutrient studie	Nutrient	Numeriek	0=geen nutrient studie, 1=nutrient 1 studie, 2= nutrient 2 studie vroeg voeden, 3=nutrient 2 studie verlaat voeden
Aantal dagen op de Intensive Care (exclusief heropname)	IC	Numeriek	

Datum van ontslag uit het ziekenhuis	Ontslag_zh	Datum/tijd	

Dagelijkse parameters

Table 5: Daily variables

Beschrijving	Veldnaam	Gegevenstype	Codering
Patiëntnummer	PatNr	Numeriek	
Datum meting	Datum	Datum/tijd	
Ziektegevoel	Ziektegevoel	Numeriek	0=geen ziektegevoel, 1=wel ziektegevoel
Lichaamstemperatuur in graden Celsius	Temp	Numeriek	
Hartslag pols	Pols	Numeriek	
Ademfrequentie per minuut van patiënt	Adem_freq	Numeriek	
Bovendruk	Tensie_boven	Numeriek	
Onderdruk	Tensie_onder		
Urineafscheiding van de patiënt	Diurese	Numeriek	0= goede diurese; 1= afwijkende diurese (<35cc per uur)
Leucocyten waarde	Leuco	Numeriek	
C-reactief proteïne waarde	CRP	Numeriek	
Amylase waarde	Amylase	Numeriek	
Bedlegerig	Bedlegerig	Numeriek	0=nee, 1=ja
Onder begeleiding op een stoel	Stoel_beg	Numeriek	0=nee, 1=ja
Onder begeleiding lopen	Lopen_beg	Numeriek	0=nee, 1=ja
Zelfstandig op een stoel	Stoel_zelf	Numeriek	0=nee, 1=ja
Zelfstandig lopen	Lopen_zelf	Numeriek	0=nee, 1=ja
Hoogste pijnscore van de dag (VAS/NRS)	Pijnscore	Numeriek	
Ontslag uit het ziekenhuis	Ontslag_zh	Numeriek	0=nee, 1=ja

Post-operatieve complicaties

Table 6: Post-operative complications

Beschrijving	Veldnaam	Gegevenstype	Codering
Aanwezigheid post-operatieve complicatie	Compl	Numeriek	0=nee, 1=ja
Type complicatie	Compl_type	Numeriek	0=geen complicatie, 1=pulmonale complicatie, 2=cardiale complicatie, 3=gastro-intestinale complicatie, 4=urologische complicatie, 5=trombo-embolische complicatie, 6=neurologische/psychiatrische

			complicatie, 7=infectie, 8=wond/diafragma, 9=chyluslekkage, 10=anders
Ernst complicatie adhv Clavien-Dindo	Compl_CD	Numeriek	
Datum van de complicatie	Compl_datum	Datum/tijd	
Is de patiënt overleden?	Overlijden	Numeriek	0=nee, 1=ja
Datum van overlijden	Datum_ov	Datum/tijd	
Reden van overlijden	Reden_overlijden	Numeriek	0=slokdarmkanker, 1=andere reden, 2=postoperatief, 3=anders, namelijk…
Reden van reinterventie	Reden_reinterventie		1=naadlekkage, 2=chyluslekkage, 3=nabloeding, 4=Fasciedehiscentie / platzbauch, 5=Intra-abominaal abces, 6=darmletsel, 7=Necrose buismaag/colon-/jejunuminterponaat, 8=pancreatitis, 9=Complicatie t.a.v. epiduraal catheter, 10=Complicatie t.a.v. jejunumfistel, 12=Geen complicatie aangetroffen, 77=anders, 99=onbekend
Pulmonale complicatie	Compl_pulmonaal	Numeriek	1=Pneumonie, 2=Pleura effusie waarvoor extra drainage, 3=Pneumothorax waarvoor behandeling, 4=Atelectase a.g.v. mucus plug waarvoor bronochscopie, 5=Respiratoir falen waarvoor re intubatie, 6=Acute aspiratie, 7=Acute Respiratory Distress Syndrome (ARDS), 8=Treacheo-bronchiaal letsel, 9=Persisterende luchtlekkage waarvoor thoraxdrain
Cardiale complicatie	Compl_cardiaal	Numeriek	0=Geen, 1= AF, 2= Decompensatio cordis, 3= AF+ decompensatio cordis, 4= AF + asystolie wv massage, 5= AF+hartinfarct+VF wv massage, 6= AF+ Astma cardiale, 7= Asystolie wv massage, 8=

			AF+cardiale ischemie, 9= Astma cardiale
Gastrointestinale complicatie	Compl_gastrointestinaal	Numeriek	0=geen GI complicatie, 1=lekkage, 2=necrose, 3=ileus, 4=obstructie, 5=jejunumfistel, 6=pyloromyotomie, 7=clostridium difficile, 8=bloeding, 9=vertraagde passage, 10=pancreatitis, 11=lever disfunctie, 12=darmletsel
Indien naadlekkage, aard naadlekkage	Aard_naadlekkage	Numeriek	0=geen naadlekkage, 1=radiologisch, 2=klinisch, 999=onbekend
Urologische complicatie	Compl_urologisch	Numeriek	0=niet urologisch, 1=nierinsuffientie, 2=nierfalen, 3=urineweg infectie, 4=urine retentie
Trombo-embolische complicatie	Compl_trombo	Numeriek	0=niet trombo-embolisch, 1=diep veneuze trombose, 2=long embolie, 3=CVA, 4=perifere tromboflebitis
Neurologische complicatie	Compl_neuro	Numeriek	0=niet neurologisch, 1=nervus recurrens, 2=andere neurologische compl, 3=acuut delier, 4=delerium tremens
Infectueuze complicatie	Compl_infectie	Numeriek	0=niet infectie, 1=wondinfectie, 2=centrale lijn inf, 3=intra-thoractaal/intra-abdominaal, 4=gegeneraliseerde sepsis, 5=andere infectie waarvoor antibiotica
Wond complicatie	Compl_wond	Numeriek	0=niet wond, 1=wonddehiscentie, 2=Fasciedehiscentie / platzbauch / hernia (acuut), 3=hernia diafragmatica (acuut)
Chylus complicatie	Compl_chylus	Numeriek	0=niet chylus, 1=type I, 2=type II, 3=type III
Andere soort complicatie	Compl_anders	Numeriek	0=niet anders, 1=overige reoperaties, 2=MODS, 3=nabloeding, 4=epiduraal catheter, 5=anders
Reinterventie	Reinterventie	Numeriek	0=nee, 1=ja, 999=onbekend
Aard reinterventie	Aard_reinterventie	Numeriek	1=radiologisch, 2=endoscopisch, 3=re-operatie
Reden voor reinterventie	Reden_reinterventie	Numeriek	1=naadlek, 2=chyluslek, 3=nabloeding, 4=Fasciedehiscenti /platzbauch, 5=Intra-abominaal

			abces, 6=darmletsel, 7=Necr buismaag/colon-/jejunum, 8=pancreatitis, 9=epiduraal catheter, 10=jejunumfistel, 12=Geen complicatie, 77=anders, 99=onbekend
Overlijden	Overlijden	Numeriek	0=nee, 1=ja
Datum van overlijden	Datum_ov	Datum/tijd	
Reden van overlijden	Reden_ov	Numeriek	0=slokdarmkanker, 1=andere reden, 2=postoperatief, 3=anders, namelijk

Heropname

Table 7: Readmission

Beschrijving	Veldnaam	Gegevenstype	Codering
Patiëntnummer ZGT	PatNr	Numeriek	
Heeft er een heropname plaatsgevonden?	Heropname	Numeriek	0=nee, 1=ja
Datum heropname	Heropname_datum	Datum/tijd	
Reden heropname	Heropname_reden	Numeriek	0=geen complicatie, 1=pulmonale complicatie, 2=cardiale complicatie, 3=gastro-intestinale complicatie, 4=urologische complicatie, 5=trombo-embolische complicatie, 6=neurologische/psychiatrische complicatie, 7=infectie, 8=wond/diafragma, 9=chyluslekkage, 10=anders
Heropname gerelateerd aan oesofagectomie	Heropname_gerelateerd	Numeriek	0=nee, 1=ja
Ernst van de complicatie bij heropname adhv Clavien-Dindo	Heropname_compl_CD	Numeriek	
Ontslagdatum bij heropname	Heropname_ontslag_datum	Datum/tijd	

Appendix 3: American Society of Anaesthesiologists' (ASA) Physical Status Classification

Table 8: American Society of Anaesthesiologists' (ASA) Physical Status Classification (16)

ASA PS Classification	**Definition**	**Examples**
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

Appendix 4: Additional graphs and tables

In order to give an overview of the daily variation of several parameters, additional graphs have been made. Figure 1 shows the daily body measurements, such as body temperature, heart rate and respiration rate. Figure 2 shows the upper and lower blood pressure. In Figure 3 the blood values C-reactive protein and leucocytes level are shown. Figure 1, 2 and 3 are specified by a group with complications and a group without complications. Figure 4 gives an overview of the amylase levels per day, specified by a group with anastomotic leakage and a group without. This distinction has been made, because the ZGT uses the amylase level to predict and detect anastomotic leakage.

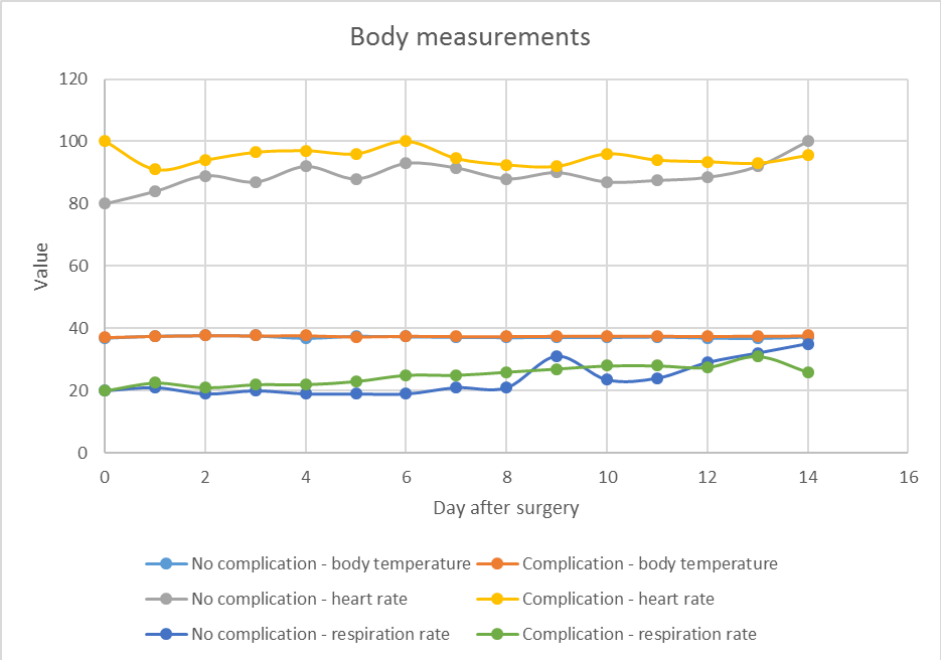

Figure 1: Body measurements (body temperature, heart rate, respiration rate) specified by complication/no complication

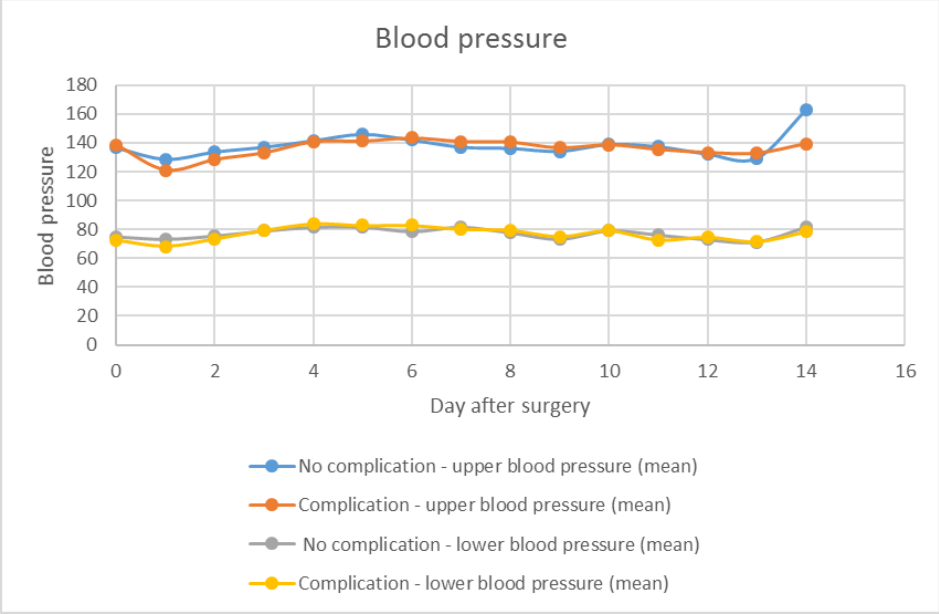

Figure 2: Upper and lower blood pressure specified by complication/no complication

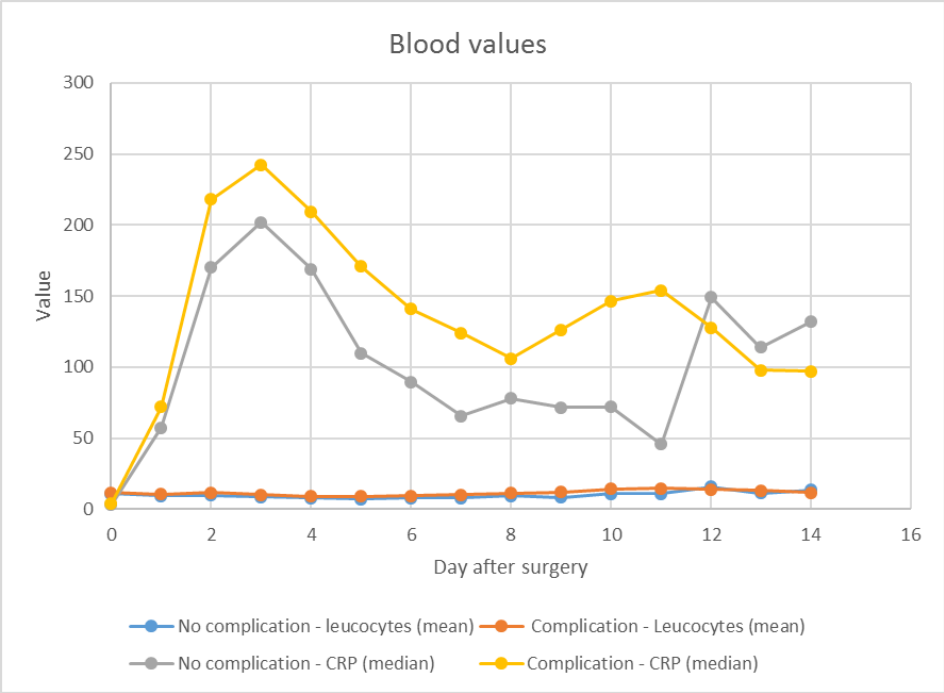

Figure 3: Blood values (leucocytes, C-reactive protein) specified by complication/no complication

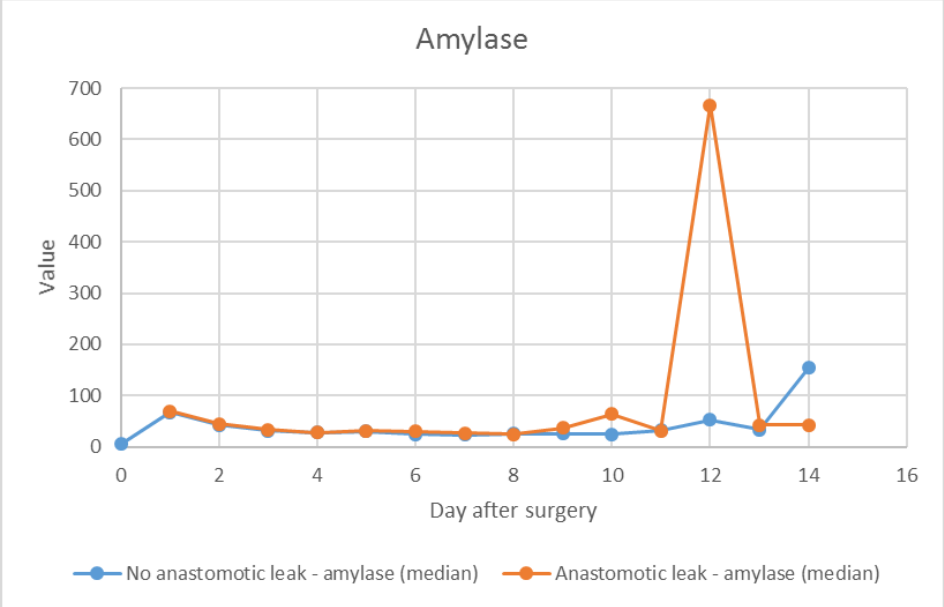

Figure 4: Amylase level specified by anastomotic leak/no anastomotic leak

In addition, an overview of the Clavien-Dindo classifications assigned to the complications has been made. Table 9 shows the complications per group, the assigned Clavien-Dindo classifications and the associated populations.

Table 9: Complications and their Clavien-Dindo classifications

Complications	**Safe discharge***	**Clavien-Dindo**		**Unsafe discharge**	**Clavien-Dindo**	
	n*	classification	n (%)	n*	classification	n (%)
Pulmonary complication	13	1	11 (84.6)	8	1	7 (87.5)
		3	2 (15.4)		2	1 (12.5)
Cardiac complication	6	1	3 (50.0)	2	1	1 (50.0)
		2	3 (50.0)		5	1 (50.0)
Gastrointestinal complication	5	1	1 (20.0)	13	3	10 (76.9)
		2	2 (40.0)		4	3 (23.1)
		3	2 (40.0)			
Urologic complication	2	1	2 (100)	1	1	1 (100)
Thromboembolic complication				1	2	1 (100)
Neurologic/psychiatric complication	2	1	2 (100)	3	1	1 (33.3)
					2	1 (33.3)
					4	1 (33.3)
Infection	1	2	1 (100)			
Wound/diaphragm	2	1	2 (100)	1	3	1 (100)
Other	2	1	2 (100)	2	3	2 (100)

*Patients with more than one complication are count for every complication they had. The number of diagnosed complications therefore differs from the number of patients.