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HOW LONG TO PROVIDE SPECIAL CARE AFTER EMERGENCY DEPARTMENT ADMISSION IN THREE MOST COMMON NON-TRAUMATIC DISEASES?

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ABSTRACT

INTRODUCTION: The first hours after the admission of patients, and proper medical care is administered in the emergency department (ED), are of decisive importance in protecting them from unexpected death. Medical staff and researchers are not consistent in the period to follow up on deaths after admission to the emergency department and they analyze arbitrarily different time intervals without any justification for the chosen period. In this study, we will conduct an epidemiological data analysis to determine the range of the most dangerous (elevated) risk (hazard) of death for patients within one month of observation from an ED admission using modern survival modeling and software.

MATERIAL AND METHODS: Epidemiological data analysis of the three most common non-traumatic diseases (neoplasms, circulatory, and endocrine) was carried out in this study. Using the 2016–2019 sample of 14,904 first-visit ED patients at the Multi-Specialistic Hospital in Gorzów Wielkopolski, Poland, we determined the range of the most dangerous (elevated) risk (hazard) of death within one month of observation, based on a Royston–Parmar (RP) regression with spline functions (assuming non-constant hazard over time).

RESULTS: The results show that in the three most common non-traumatic diseases (neoplasms, circulatory, and endocrine) for the first 72 hours, patients should be under special supervision of medical personnel to avoid an excess of unexpected deaths. Moreover, within a month from ED admission, the hazard ratio (HR) of death was almost half as high [HR = 1.47, 95% confidence interval (CI) = 1.07 to 2.02] in diagnosed circulatory patients and over twice as high (HR = 2.25, 95% CI = 1.58 to 3.20) in neoplastic diseases as compared to reference endocrine patients. Moreover, the estimated RP hazards (probabilities of death) increased until the third day after admission, reaching 1.0% (95% CI = 0.8% to 1.4%) of endocrine patients, 1.5% (95% CI = 1.3% to 1.6%) of circulatory patients, and 2.2% (95% CI = 1.8% to 2.6%) for neoplasms, and then dropped radically with the time of observation.

CONCLUSIONS: In view of the care of patients in the three most non-traumatic clinical diagnoses (endocrine diseases, circulatory diseases, and neoplasms), special attention should be paid to the first three days after admission to the ED (after this time, in the first month of observation, the risk of death of these patients decreases significantly).

KEYWORDS: emergency department; non-traumatic diseases; death; Royston–Parmar model

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INTRODUCTION

It can certainly be said that the first hours after admission of patients, and proper medical care administered in the emergency department (ED), are of decisive importance in protecting them from unexpected death (see, e.g. [1]). And so French researchers were wondering if unexpected deaths within 72 hours of an emergency department visit were preventable and they concluded, based on their sample, that the rate of unanticipated death within three days of an ED visit is 85 per 100,000 admissions and more than half of the unexpected deaths were related to a medical error that could have been prevented [1]. However, it is puzzling why the authors chose these 72 hours of observation and not another. Unfortunately, they do not explain this and it gives the impression that it was arbitrarily determined.

As cited in their paper, specific causes of mortality were not taken into account, and they considered all causes [1], in contrast, in the very current study by Reaven et al. [2], only deaths of patients from septic shock were evaluated at regular intervals 24 (5.5%), 48 (9.5%), and 72 hours (11.5%), after admission to the emergency department.

In turn, a seven-day observation period considered qualitative factors in patients who died shortly after an emergency department discharge was described by Gabayan et al. [3, 4]. In the latter study, the authors emphasize the importance of such analysis because early death after an ED discharge may signal opportunities to improve care and to identify patient and process of care-level themes that may provide possible explanations for early post-discharge mortality [4]. Based on a large research sample (nearly 300,000 patients and nearly 450,000 discharges), the authors observed that 0.05% of deaths occurred within 7 days of an ED discharge.

Stretching the observation period, deaths within 8 days after discharge were studied by Gunnarsdottir & Rafnsson [5]. In this sample, a non-causative diagnosis had been given to 11% of those who died within 8 days after discharge, while the mortality rate per 100,000 within 8 days was 208.5, within 15 days 347.4, and 30 days 648.6.

Based on a retrospective chart review, an eight-day follow-up of deaths of 2,665 medical examiner cases of patients after discharge from an ED was also conducted by Kefer et al. [6]. In the sample, the authors estimated the death rate in Milwaukee County of discharged patients was 13 per 100,000 and found death after discharge from an ED was uncommon.

Since death rates are an outcome that can be used to describe a service, Baker & Clancy [7] measured mortality rates within 30 days of discharge from an emergency department, or within 30 days of admission to an emergency department. The rates were 0.19% for those discharged, 4.6% for those admitted, and 0.27% for those patients who died while in an ED [7]. However, this study did not use sophisticated statistical tools and relied only on simple fractional calculations. Anyway, the authors believe that their numbers are sufficient to describe the outcome of an ED's services.

As can be seen from this brief review of the literature, medical staff and researchers do not agree on the length of the period to follow-up on deaths after admission to an emergency department and they arbitrarily analyze different time intervals without any justification for the chosen period. Also, the justification for the observation period can be trivial and unsupported by any reasonable scientific premise (e.g. [4] explain that "we chose the 7-day time frame because of its clinical relevance, implications for health policy decisions, and prior use in related studies", or [5]: "deaths within 8 days after discharge have, in previous studies, been evaluated retrospectively based on review of hospital records and the cause of death"). There is still no answer to the question: What is the period of treatment and observation of patients that are the most important for their survival from the moment they report to an emergency department?

Since the core mission of emergency medicine is to provide immediate care to acutely ill and injured patients [8], to extend the scope of ED observations, in this study we will conduct an epidemiological data analysis to determine the range of the most dangerous (elevated) risk (hazard) of death for non-traumatic patients within one-month of observation from an ED admission using modern survival modelling and software.

MATERIAL AND METHODS

We conducted a 2016–2019 single-center retrospective study from non-traumatic medical records and electronic data in the emergency department at the 1,000-bed public Multi-Specialistic Hospital in Gorzów Wielkopolski, Poland. Monthly, the hospital has 1,200 admissions to the ED as ascertained from the codes of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD10) [9].

We aimed to investigate the top three (most frequent) ICD10 non-traumatic diagnoses and 1- and 31-day mortality rates of patients after an ED contact (we chose this approach in order not to underestimate short-term mortality). In our study, the mortality day was defined as death on the same day as death registration, since death registration is available only by date and not by time of day.

Only the history of unduplicated patients after the first ED visit during follow-up was included in the statistical analysis. Using a sample of 14,904 patients (both living and deceased), we calculated the percentage of death in patients who died within one month from the first visit to an ED (subjects were restricted to age 18 years and older because of the inherent differences between pediatric and adult presentations and outcomes as well as due to taking into account the low probability of developing chronic diseases in younger patients; the cause of death was obtained from a nation-wide registry by record linkage from electronic administrative databases). Consequently, the highest percentage of deaths were within chapters 'Neoplasms' (12.3%), 'Circulatory' (8.5%), and 'Endocrine' diseases (3.9%). A graphical presentation of death ratios (= disease deaths/all deaths) during the month of observation is shown in Figure 1.

The lines attached in Figure 1 roughly show that the highest percentage of deaths in the three selected diagnoses (neoplasms, circulatory, and endocrine diseases) is observed in the first week after admission to an ED, and after two weeks this rate is close to zero.

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Bioethical Committee (BC) of the District Medical Council in Zielona Góra, Poland (ref. 25/107/2018). Since the current study was retrospective and the subjects were de-identified, the BC waived the need for written consent.

Methods

Modeling of the censored survival data is preferably conducted by a Cox proportional-hazards regression. Because the Cox model is not without limitations, for example in the case of complex data, non-proportional hazards are a potential difficulty (when monotonicity of the survival function is affected in the region where the observed data are sparse; in regions where data are dense, monotonicity is effectively imposed by the data themselves). Then parametric approaches can be advantageous (even the originator of the Cox model has expressed a preference for parametric modeling, see [10]), and a Royston–Parmar (RM) approach [11] may be a reasonable alternative, which fits a restricted cubic spline to flexibly model the baseline log cumulative hazard on the proportional hazards scale. This feature incorporates time-dependent effects and permits measures of the hazard rates to be estimated at all time points (an important feature when using the model; despite the apparent advantages of the RP model, it is not widely used in health research [12]).

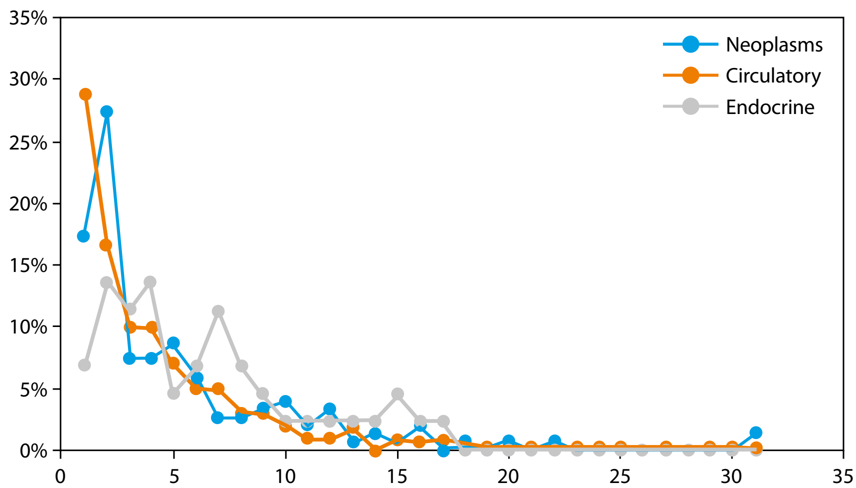

FIGURE 1. Death ratios in the selected ICD10 chapters since an emergency department (ED) admission

Table 1. The estimated hazard ratios between the selected ICD10 chapters, *i.e.* endocrine diseases, circulatory diseases, and neoplasms, and an ED within one month of observation

ICD10 chapter	HR	95% CI	p value
Endocrine diseases	1.00 (ref.)	–	–
Circulatory diseases	1.47	(1.07, 2.02)	0.0162
Neoplasms	2.25	(1.58, 3.20)	< 0.0001

CI — confidence interval; HR — hazard ratio

The novelty of this attractive approach relies on the fact that the survival function S(t) transformed by a link function g(.) is smoothed on the log time (t) scale against anticipated artifacts in the fitted spline functions that would be more severe for the hazard function. As a result, a class of such models can be created

$$g[S(t;z)] = g[S_0(t)] + \beta^T z,$$

where $S_0(t) = S(t;0)$ is the baseline survival function and β is a vector of parameters to be estimated for covariates z. In the spline-based survival RP model, a transformation $g(S_0(t,z))$ leads to some non-linear functions $s(x, \gamma)$, where $x = \log(t)$, having an adjustable parameter vector γ. The complexity of the model, thus the dimension of γ, is governed by the number of knots in the spline function s(.) [11].

Package ‘flexsurv’ [13] for R statistical platform [14] allows parametric distributions to be fitted to survival data, gaining the convenience of parametric modeling. Built-in choices include spline-based models with any number of knots and parameter-generalized gamma and F distribution families [11].

RESULTS

The presented results could not have been obtained otherwise than by using the Royston–Parmar spline regression model. In this study, the interpretation of statistical results is based on the classical hazard ratio (HR), which is the probability of an event in comparison groups relative to the reference group probability over a unit of time (this ratio is an effect size measure for time-to-event data).

Using the ‘flexsurv’ package, the estimated HRs of early death between the selected ICD10 chapters, *i.e.* endocrine diseases, circulatory diseases, and neoplasms, and in an ED within one month of observation are reported in Table 1. Based on the collected HRs it can be stated that the risk of an early death for patients at the analyzed ED is the lowest for patients with endocrine diseases, about half of it is higher for circulatory diseases, while the top rates are recorded for neoplasms.

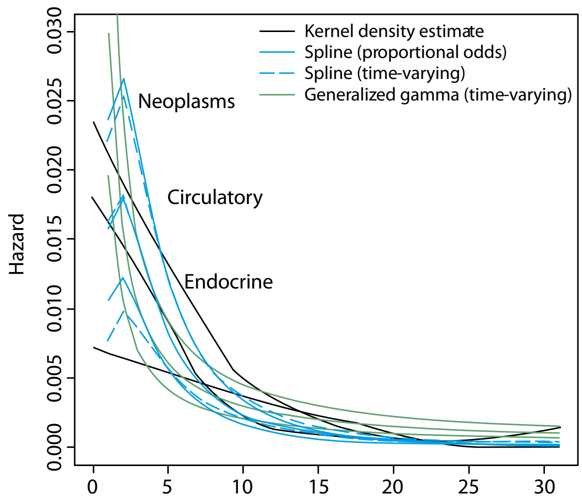

FIGURE 2. Hazard curves of death of patients vs days after admission to the emergency department

The plot of the estimated Royston–Parmar hazard (probability of death) after admission to the ED, created in the ‘flexsurv’ package, is presented in Figure 2.

The modeled RP hazard curves in Figure 2 increased until the third day after admission, reaching 1.0% (95% CI = 0.8%, 1.4%) hazard of endocrine patients, 1.5% (95% CI = 1.3%, 1.6%) of circulatory patients, and 2.2% (95% CI = 1.8%, 2.6%) for neoplasms, and then dropped radically with the time of observation. It can also be seen that the course of the hazard curves in Figure 2 is similar to the death ratios in Figure 1.

DISCUSSION

Proper medical care administered in the emergency department is of decisive importance in protecting patients from unexpected death. Following the literature, however, the time of observation of the risk of unexpected events is undetermined, inconsistent, and chosen arbitrarily.

Since emergency departments handle a large proportion of traumatic patients with orthopedic fractures and other bodily injuries as a result of road accidents and workplace accidents, or violence to a person, etc., (these cases are often classified as acute, and patient survival a priori has no causal relationship with their previous lifestyle and chronic disease status), it seemed equally attractive to us to deal with non-traumatic cases. Hence, in our study, the same data that was originally used in a study [9] to predict acute mortality in emergency department patients based on selected hematological biomarkers (the huge and only partially exploited set of these data was an incentive to continue research on the survival of patients admitted to ED), we decided to analyze in a brand-new observational study. Although, the downside of the research material collected is the lack of precise data on the cause of death of the patients. However, due to the short observation time, we trust that it did not deviate significantly from the patients' diagnosis specified by the ED (also, the lack of ED discharge times is a limitation of this study, however, it is difficult to say whether it had any impact on fatal clinical events, as well as medical misdiagnoses, which were also not investigated in this study).

Still, in our study, we found that with the help of commonly available methods and software, it is possible to precisely determine the time of special care for patients from the time of their admission to the ward. Moreover, the premise for such modeling as with the RP method may be the calculation of simple ratios of adverse events to all cases (in our study, fatalities). It seems that our statistical proposal is correct because a query of scientific publications made us realize the following.

After researching articles on patient deaths after admission to the emergency department, it is safe to say that most of them are based on survival analysis using the Kaplan–Meier method. This was the case with, for example, an analysis of the two-month survival of patients with congestive heart failure without hospital readmission reported by Chin & Goldman [15], for patients with and without visits to the emergency department for self-harm, suicide attempts, or an overdose [16], about the long-term mortality in older hospitalized patients with and without delirium within six months after an ED visit [17], and in three hundred French medical patients aged 80 during several years of observation [18], or in the much shorter five-day timeframe in adults with septic shock relative to time from an emergency department triage [2]. A methodologically different statistical perspective on the mortality of patients in a pediatric emergency department at a tertiary medical center in China had Zhu et al. [19], presenting deaths in three subgroups of children: on arrival, within 24 hours, and over 24 hours after ED admission by several types of diseases/disorders. However, it seems that all the analyzed time intervals were created arbitrarily and have no practical significance, e.g. in reducing premature deaths of patients and focusing on the most important period of clinical observation and treatment after an ED admission. For this purpose, an unsurpassed statistical solution seems to be RP regression with spline functions, whose importance, still underestimated by the medical world, may play a huge role in recognizing and assessing "sensitive" risk periods of observation of patients.

In our study, this statistical time result can be obtained in, for example, the 'flexsurv' R package which is easy to use for practitioners. We trust that this idea can be successfully used in the analysis of other clinical responses over time. There remains the question of explaining the causes of such a confirmed epidemiological situation, but this is a problem for another scientific clinical study.

CONCLUSIONS

Based on the collected statistical material and the results obtained, the following conclusions can be drawn:

1. A review of the literature indicates the assumption of an arbitrary observation period of patients admitted to an ED and the lack of standardization in order to protect patients from unexpected health effects.
2. A Royston–Parmar regression with the use of 'flexsurv' R package spline functions allows for an original, reliable, and precise assessment of the risk ranges of the occurrence of the analyzed clinical response and can be used in a wide research spectrum.
3. For selected ICD10 chapters, *i.e.* endocrine, circulatory, and neoplasms, this technique used the indicates an increase in patient mortality up to the third day after admission to an ED. Until then, patients should be under special supervision of medical personnel in order to avoid an

excess of unexpected deaths After this period the risk of death decreases radically.
4. Attempts at longer observation periods do not statistically significantly improve the statistics of sudden deaths after admission to the hospital ED.

Article information and declarations

Data availability statement

All datasets an R codes used in the analysis are shared as part of this publication.

Ethics statement

This study was carried out in accordance with the Declaration of Helsinki and was approved by the Bioethical Committee (BC) of the District Medical Council in Zielona Góra, Poland (ref. 25/107/2018). Since the current study was retrospective and the subjects were de-identified, the BC waived the need for written consent.

Author contributions

Wawrzyniec Mantorski, Piotr Feusette, Andrzej Tukiendorf, and Edyta Wolny-Rokicka were involved in study concept, interpretation of the data, and in critical revision of the manuscript for important intellectual content. Edyta Wolny-Rokicka (previously employed at the Multi-specialist Hospital in Gorzów Wielkopolski, Poland) was involved in acquisition of the data. Andrzej Tukiendorf provided statistical expertise.

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Conflict of interest

The results of the study and their possible publication do not result in any conflict of interest.

Supplementary material

None.

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