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ORIGINAL ARTICLE - NEUROSURGERY GENERAL

The Danish chronic subdural hematoma study—predicting recurrence of chronic subdural hematoma

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Abstract

Background An increasing incidence of chronic subdural hematoma (CSDH) and an unchanging high recurrence rate of 10–20% call for individualized treatment. The aim of this study was to establish individualized prediction models for the risk of recurrence treating death as a competing risk.

Methods A retrospective national cohort of unilateral CSDH was included for analysis. Using competing risk survival analysis, we tested whether available covariates were associated with the risk of recurrence. We further established a pre- and a postoperative prediction model, where predictors were chosen using a LASSO approach. The models were visualized in nomograms. Predictive performance was evaluated by c index and calibrations plots.

Results A total of 763 patients with surgically evacuated unilateral CSDH were included for analysis. The recurrence rate was 14% while 12% of patients died during follow-up (1 year). In our association model, hematoma size, drain type, drainage time, presence of complications, and Glasgow Coma Score were significantly associated to recurrence. Subdural drain was associated with a lower recurrence risk than subgaleal drain. The preoperative model included hematoma size, hematoma density, and history of hypertension. The postoperative model included further drain type, drainage time, and surgical complications.

Conclusion The nomograms allow easy assessment of the recurrence risk for the individual patient, providing a better possibility for individual adjustment of treatment and follow-up. The predictive performance indicates that significant unaccounted or unknown factors still remain. The association test found passive subdural drain superior to passive subgaleal drain in minimizing the risk of CSDH recurrence.

Keywords Chronic subdural hematoma · Recurrence · Prediction model · Postoperative drain

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Introduction

The recurrence rate of chronic subdural hematoma (CSDH) after surgical management of CSDH ranges from 5 to 30% [1, 17, 19, 27]. Numerous studies have used association models in their search for risk factors of recurrence yielding various suggestions of causalities [5, 16, 18, 26]. Recent studies have focused on prediction models for the recurrence of CSDH [12, 23], aiming at establishing a prognostic grading system to predict the risk of recurrence for the individual patient. These studies are based on small patient cohorts ($n = 107$–331) and none of them are considering death as a competing risk factor to recurrence.

A grading system to predict postoperative recurrence, with high internal and external validity, has several valuable purposes, such as enabling clinicians to make individual risk-benefit assessments concerning choice of surgical procedures, postoperative care, and follow-up. This is well in line with the current focus on personalized neurosurgical care.

In this study, we employ classical association analysis and propose a prediction model for recurrence of CSDH based on a large national retrospective patient cohort.

Materials and methods

Study population and variables

The study population was retrieved from a retrospective multicenter study of a national patient cohort involving all neurosurgical departments in Denmark: Rigshospitalet University Hospital, Odense University Hospital, Aarhus University Hospital, and Aalborg University Hospital. All patients admitted to one of these neurosurgical departments with the ICD-10 diagnosis code of CSDH between January 1, 2010, and December 31, 2012, were included ($N = 763$) and followed 1 year after surgery for the outcomes of recurrence of CSDH or death. All parameters were recorded on site from electronic patient records by the first author (NCAR). In the present study, only unilateral CSDH was included for analysis. Bilateral CSDH has been analyzed in a previous study [2].

Clinical data included age, sex, comorbidities (diabetes and hypertension), previous craniotomy, anticoagulant and antiplatelet treatment, and Glasgow Coma Score (GCS). Radiological data were obtained on preoperative cerebral CT scans. The size of the hematoma was calculated by the XYZ method [25]. Midline shift was measured from septum pellucidum to the sagittal suture. Size and midline shift were analyzed untransformed as well as logarithmized. Atrophy was estimated as a ratio of the total brain parenchyma width to the intracranial diameter. Hematoma density was classified into four groups: homogeneous, separated (as described by Nakaguchi et al. [17]), mixed, and membranous. The membranous type was defined as a hematoma with homogenous content and membranes (septae) running from the inner to the outer membrane, while the mixed type was defined as a hematoma with mixed hypo- and hyperdense content. Surgical data included surgical procedure (one–burr hole craniostomy, two–burr hole craniostomy, or craniotomy), drain type (subdural, subgaleal, or no drain), drainage time (0, < 12 h, ≥ 12 h, ≥ 24, ≥ 48), and surgical complications (yes/no). Surgical complications included bleeding, infection, postoperative seizures, and retreatment due to bleeding or insufficient hematoma evacuation. Retreatment during primary hospital admission was not registered as recurrence. Recurrence was defined as re-accumulation of CSDH requiring surgical evacuation after discharge from primary treatment.

Statistical analysis

The primary outcome of this study was the time to recurrence of a CSDH in need of surgical retreatment (recurrence). As it is expected that a relevant portion of patients die during follow-up, death was considered a competing risk.

The standard analysis of time to event data focuses on survival function and hazard rate (HR). Kaplan-Meier curves are nonparametric estimates of the survival function or, equivalently, its counterpart the cumulative incidence function (CIF). The CIF for a given point in time is the probability of the event (death or recurrence) to take place up to then.

The Cox proportional hazards model is a rate model used to relate explanatory variables to the hazard rate, which in turn implies how these variables relate to the survival function or CIF.

In the presence of competing risks, these standard estimates can be biased, when treating competing events as censored observations (Kaplan-Meier curves will then overestimate the chance to survive). Therefore, for this study, we applied methods tailored to time to event data in the presence of competing risks. We calculated nonparametric Aalen-Johansen estimates of the CIF of recurrence and death.

Association of time to recurrence with variables

Using Fine and Gray's regression model, we investigated whether time to recurrence is associated with any of our variables. Fine and Gray model the subdistribution hazard rate (SH) for recurrence and effects of covariates are quantified in terms of subdistribution hazard ratios (SHRs). We refer the reader to the supplementary material (Analytical considerations) for further elaboration of these terms and concepts. Each of the 15 variables was tested in a separate regression model. Age and gender were considered as possible confounders and included in all regression models. For categorical variables, the Wald test was used to test the global hypothesis of no effect or the hypothesis of no difference between the effects of different categories. Although GCS is of ordinal nature, we considered it an approximately continuous variable in all our analyses in favor of a larger number of degrees of freedom. Plots of Schoenfeld residuals were used to assess the proportionality assumption incorporated in the Fine and Gray model, i.e., the assumption that the effects of explanatory variables on the SH do not change with time.

We used a 5% significance level. To take multiple testing into account and control the family-wise error rate, we applied Bonferroni's method. However, this method is rather conservative in our case since not all of our variables are independent from each other.

Prediction recurrence

To build a prediction model for the time to recurrence, we used Fine and Gray's model together with a group LASSO penalty [4, 8]. Penalized regression methods can handle large numbers of predictors despite of a relatively small effective sample size. The LASSO penalty is frequently used for variable selection. The group version of the penalty assures that variables corresponding to different levels of a categorical predictor are selected together. Moreover, the penalty was constructed such that size and its logarithm (as well as midline shift and its log) was selected either in or out together. The tuning parameter controlling the strength of the penalty was chosen to maximize the goodness-of-fit in cross validation procedure. As goodness-of-fit-measure, we used the generalized cross validation criterion. Variable standardization prior to fitting was applied, but reported coefficients are returned on the original scale. We performed a complete case analysis, i.e., only used data from patients without missing values in any of the included predictors. Predictor selection through this approach is known to be sensitive to the specific dataset. To make the results of the LASSO method more stable, we applied stability selection [14] in the modified version suggested by Mogensen et al. [15]. We repeated the procedure 100 times on random subsets of our data with half of the sample size. The predictors whose coefficients were not shrunk to 0 in at least 50% of the repeats were chosen to be included in the final model. They were then used to fit an ordinary (without penalty) Fine and Gray regression model, which constitutes the final prediction model.

As potential predictors, we considered all available clinical, radiological, and surgical variables. We investigated two different models regarding the predictors used: (A) a postoperative model relying on all of the mentioned predictors and (B) a preoperative model using only those predictors that were available before surgery. We calculated and plotted model-based predictions for major predictors contained in our prediction models, and visualized the prediction model with the help of nomograms [10, 29].

The performance of our prediction models was evaluated using the c index for specific points in time [10, 28] and calibration plots (supplementary material).

The c index is the concordance probability indicating to what extent observed times to recurrence reflect the same order as corresponding predictions, having a value of 0.5 if predictions are random (coin tossing) and 1 if the model discriminates perfectly. The c index is a generalization of the area under the ROC curve (AUC). We calculated the apparent c index (using the data that has been used to build the model for validation). As obtained values are known to be overly optimistic, we also calculated a bootstrap cross validated c following the strategy described in Steyerberg [24]. Here, the prediction models were trained on 1000 bootstrap samples drawn with replacement from the original data and having the same size. The models were then assessed using the observations not contained in the bootstrap sample to calculate an optimism-corrected c.

Whereas the c index measures the discriminative ability of a prediction model, we used calibration plots to assess the agreement between observations and predictions [9]. That is, if we for example predict a 10% risk for recurrence within a specific time period, the observed frequency of recurrences should be close to 10% amongst all patients with the same prediction if the prediction model is well calibrated. One apparent calibration plot relies on our original data and a second plot was based on 1000 bootstrap samples, whereby the model again was trained on the bootstrap samples and validated in the corresponding observations not contained in the bootstrap samples.

Statistical analyses were performed with R version 3.3.2 together with the packages cmprsk version 2.2-7, riskRegression version 1.3.7, pec version 2.5.3, aod version 1.3, crrp version 1.0, rms version 5.1.1, and tableone version 0.0.8.

Results

Table 1 outlines the basic characteristics of our study population.

Out of the 763 patients, 107 (14%) experienced recurrence and 95 (12%) died during follow-up (1 year post-surgery). From the total number of patients, 727 patients (95%) had complete observations for all predictors. Only complete observations were included in our prediction model.

Table 1 Basic characteristics of the study population

	Patients, *n* (%)	Missing (%)
No. of patients	763	
Event (%)		0.0
Alive (1 year after surgery)	561 (73.5)	
Recurrence	107 (14.0)	
Death	95 (12.5)	
Clinical variables		
Gender (female) (%)	216 (28.3)	0.0
Age (mean ± SD)	72.4 ± 12.5	0.0
Comorbidities (%)		
History of hypertension	244 (32.0)	0.0
History of diabetes	106 (13.9)	0.0
Previous craniotomy	20 (2.6)	0.0
Drug history (%)		
Anticoagulation treatment	149 (19.5)	0.0
Antiplatelet treatment	248 (32.5)	0.0
History of head trauma (%)	369 (48.4)	0.1
GCS (mean ± SD)	13.9 ± 2.0	3.7
Radiological variables		
CT hematoma size, cm^3 (mean ± SD)	130.8 ± 50.0	0.1
Midline shift, mm (mean ± SD)	9.5 ± 4.5	0.4
Atrophy, ratio (mean ± SD)	84.3 ± 11.7	0.3
Density (%)		0.1
Homogenous	272 (35.7)	
Separated	64 (8.4)	
Membranous	222 (29.1)	
Mixed	204 (26.8)	
Surgical variables		
Procedure (%)		0.0
1–burr hole craniostomy	683 (89.5)	
2–burr hole craniostomy	21 (2.8)	
Craniotomy	59 (7.7)	
Drainage (%)		0.0
No drain	22 (2.9)	
Subdural drain	319 (41.8)	
Subgaleal drain	422 (55.3)	
Drainage time in hours (%)		0.5
0	22 (2.9)	
1–23	96 (12.6)	
24–47	481 (63.4)	
≥ 48	160 (21.1)	
Surgical complications (%)	71 (9.3)	0.1

Figure 1 shows nonparametric estimates of the CIFs for recurrence and death. The probability for recurrence increased during the first 3 months after which it reached a constant level of approximately 0.14 (14%). Deaths occurred more evenly spread during the 1-year follow-up and reached an overall probability of roughly 0.12 (12%) at the end of follow-up.

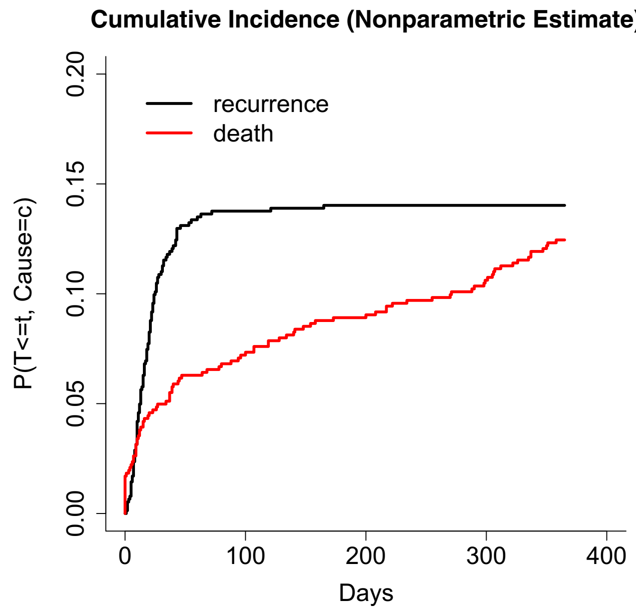

Fig. 1 Nonparametric estimates for the cumulative incidence function of recurrence and death

Association of time to recurrence with study variables

Table 2 shows the results from the association analyses. Based on plots of Schoenfeld residuals, hematoma size and midline shift were used as logarithmized variables (using base 2). The following variables were significantly associated at a 5% level: $\log_2$-size, drain type, drainage time, presence of complications, and GCS. The SHR for $\log_2$-size was 2.0 (95% CI 1.3–3.0) corresponding to a 100% increase in SH for each doubling in size. Subdural and subgaleal drains decreased the SH by 70% and 40% respectively when compared with no drain (SHR = 0.3, 95% CI 0.1–0.8 and SHR = 0.6, 95% CI 0.2–1.3). The difference between the SHRs for subdural and subgaleal drains was significant (Wald test *P* value = 0.03). Further, compared with no drain, a drainage time of 1–23 h, 24–47 h, and at least 48 h lowered SHs by 10% (SHR = 0.9, 95% CI 0.4–2.1), 60% (SHR = 0.4, 95% CI 0.2–1.0), and 70% (SHR = 0.3, 95% CI 0.1–0.8) respectively. Finally, the presence of complications increased the SH by 90% (SHR = 1.9, 95% CI 1.1–3.2) and each increase in GCS by one unit lowers the SH by 10% (SHR = 0.9, 95% CI 0.9–1.0). Only $\log_2$-size remained significant after applying Bonferroni's conservative correction for multiple testing.

Predicting recurrence

Model A in Table 3 shows the variables contained in our prediction model when using all predictors available before and after surgery (postoperative model). The predictors selected by the stability selection were size as well as $\log_2$-size,

Table 2 Association with time to recurrence. The table contains subdistribution hazard ratios (SHR) for the investigated variables. All regression analyses included additionally age and gender. Effects that are significant at a 5% level are shown in italics

Predictor	SHR	95% CI	*P*
Clinical variables			
History of hypertension	1.4	1.0–2.1	0.08
History of diabetes	1.3	0.8–2.2	0.25
Previous craniotomy	1.6	0.6–4.3	0.35
Anticoagulation treatment	0.9	0.6–1.5	0.72
Antiplatelet treatment	0.9	0.6–1.4	0.58
History of head trauma	0.9	0.6–1.3	0.50
GCS	0.9	*0.9–1.00*	*0.05*
Radiological variables			
Log_2(size)	2.0	*1.3–3.0*	*< 0.01*
Log_2(midline shift)	1.2	0.9–1.5	0.19
Atrophy	1.0	1.0–1.0	0.17
Hematoma density (vs. homogeneous)			0.08
Separated	1.8	1.0–3.3	
Membranous	1.0	0.6–1.7	
Mixed	0.8	0.5–1.3	
Surgical variables			
Surgical procedure (vs. 1–burr hole craniostomy)			0.55
2–burr hole craniostomy	1.0	0.3–3.1	
Craniotomy	1.4	0.8–2.7	
Drain type (vs. no drain)			*0.02*
Subdural drain	0.3	0.1–0.8	
Subgaleal drain	0.6	0.2–1.3	
Drainage time in hours (vs. 0 h)			*< 0.01*
1–23	0.9	0.4–2.1	
24–47	0.4	0.2–1.0	
≥ 48	0.3	0.1–0.8	
Surgical complications	1.9	*1.1–3.2*	*0.03*

Table 3 Variables selected by the LASSO logistic regression for models A: postoperative model and B: preoperative model. The table shows estimated subdistribution hazard ratios and their 95% confidence interval obtained from an ordinary Fine and Gray regression model using the selected variables. Hazard ratios correspond to the variables' original scale

	Model A: Postoperative model		Model B: Preoperative model	
Predictor	SHR	95% CI	SHR	95% CI
Log_2(size)	2.1	1.4–3.3	2.0	1.3–3.1
Hematoma density (vs. homogenous)				
Separated density	1.6	0.9–2.8	1.6	0.9–2.9
Membranous density	0.8	0.5–1.4	1.0	0.6–1.6
Mixed density	0.7	0.4–1.2	0.8	0.5–1.3
History of hypertension (yes)	1.5	1.0–2.2	1.4	1.0–2.1
Drain (yes)	0.6	0.3–1.5		
Subgaleal drain	1.5	0.9–2.3		
Drainage time (h)				
24–47	0.6	0.4–1.0		
≥ 48	0.4	0.2–0.9		
Surgical complications	2.0	1.2–3.5		

density type, history of hypertension, drain type, drain time, and presence of complications. In the final model (Table 3), size was omitted in favor of $\log_2$-size based on residual plots and in order to have a simpler model. Although density type and a history of hypertension were not significantly associated with time to recurrence in the association analyses, they did turn out to improve prediction quality in our dataset.

In terms of cumulative incidences (CIF) for recurrence, larger hematoma size, surgical complications, and a history of hypertension translated into higher predictions for the incidence of recurrences. Not having drain leads to a higher prediction than subgaleal drain, which still had a higher prediction of CIF than subdural drain. The hematoma densities could be ordered as follows according to their predicted CIF: separated, homogenous, membranous, and mixed, whereby separated density leads to higher prediction of recurrence and mixed density leads to the lower prediction of recurrence.

Corresponding model-based predictions illustrating the effects of different sizes (Fig. 2a) and drains (Fig. 2b)are shown in Fig. 2. Further, Fig. 3a and b contain nomograms visualizing our prediction models, which enables the reader to calculate the predicted risk of recurrence within 12 weeks for an arbitrary patient.

In model B (preoperative model), only predictors available before surgery were used. The model selection by the LASSO method selected the same predictors apart from drain type, drain time, and presence of surgical complications. The direction of the effects of the different predictors on the CIF is the same as in model A.

We evaluated the discriminative performance of our prediction model A at 30, 60, and 90 days and obtained an apparent c index of 0.67, 0.68, and 0.67 respectively in our sample. As the sample had already been used for model selection, this estimate of model performance is overly optimistic. By bootstrapping, we obtained an optimism-corrected c index of 0.63 at all considered times.

For the model B using only pre-OP predictors, apparent c indexes were as expected lower and approximately equal to 0.64, 0.64, and 0.63 for 30, 60, and 90 days. Optimism-corrected c indexes were equal to 0.60, 0.61, and 0.60.

The calibration plot comparing observed and predicted frequencies of recurrence after 12 weeks showed reasonably good calibration for our dataset for predicted recurrence probabilities (from model A) below roughly 30–40%. For higher predicted probabilities, observations were too rare in order to get a meaningful estimate. The calibration plot based on 1000 bootstrap samples still showed relatively good calibration with some under/overestimation for lower and higher predictions, respectively. The latter suggests that the optimism contained in the apparent calibration performance of our model is only minor. The apparent as well as bootstrap validated calibration

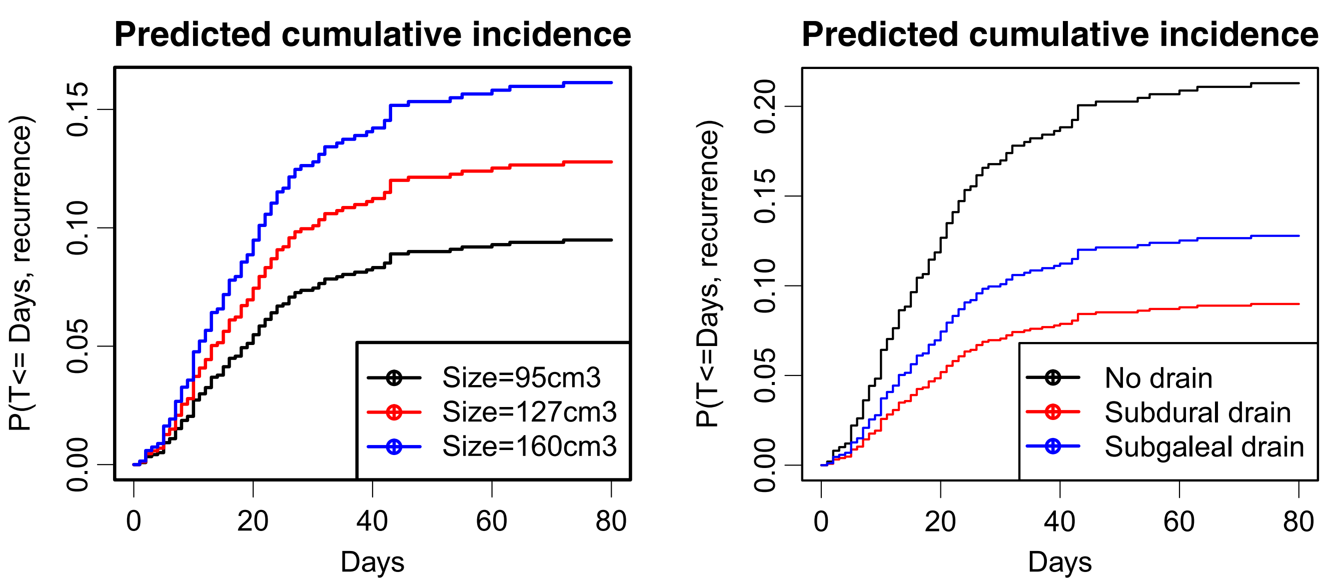

Fig. 2 Model-based predictions of the predicted cumulative incidence of recurrence, illustrating the impact of hematoma size and drain type, assuming no hypertension, homogenous hematoma density, drainage time between 24 and 47 h and no surgical complications. **a** Predicted cumulative probability of experiencing recurrence within 80 days after surgery for patients with varying hematoma sizes, assuming drain type to be subgaleal drain. The figure illustrates how increasing size of the hematoma increases the probability of experiencing recurrence. A hematoma size of 95 cm^3 has a predicted cumulative incidence of experiencing recurrence of approximately 10%, while a hematoma of 160 cm^3 has a probability of experiencing recurrence of 16%. **b** Predicted cumulative probability of experiencing recurrence depending on the drain type, assuming a hematoma size of 127 cm^3. Patients not treated with drain have a significant increased predicted probability of experience recurrence compared with patients with either subdural or subgaleal drain corresponding to 21% at the end of 80 days post surgery. Subdural placement is superior to subgaleal placement of the drain when comparing the predicted probability of experiencing recurrence being approximately 12% for subgaleal drain and approximately 7% for subdural drain

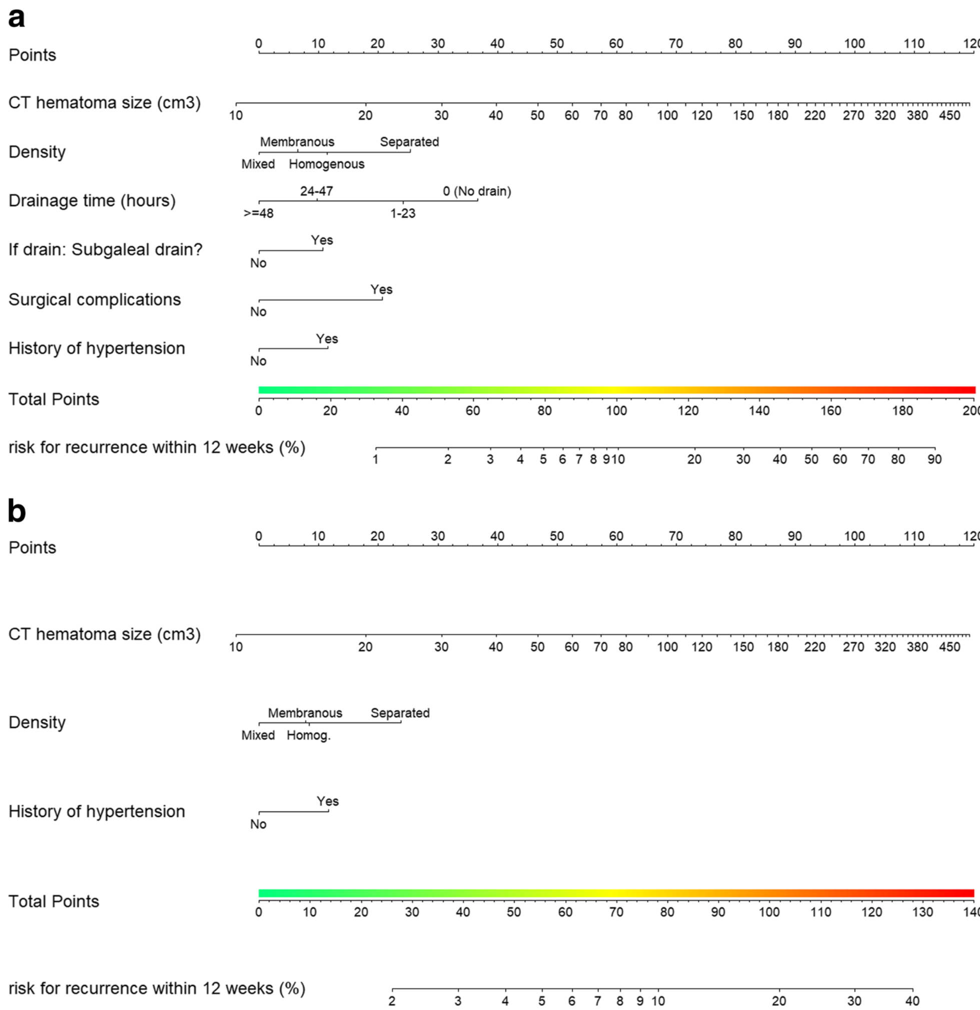

Fig. 3 Nomograms to calculate model-based predictions for the risk of recurrence within 12 weeks (based on models A and B). For each variable contained in the prediction model (e.g., hematoma size): Find a patient's value on the corresponding axis to determine how many points the patient receives for this variable (by drawing a straight line upwards to the "Points"-axis). Add all these points and find the overall sum on the "Total Points" axis. Calculate the patient's predicted risk for recurrence within 12 weeks on the below axis by going straight down. The color scale serves as rough indication for the corresponding risk level

of model B was similar to that of model A. Calibration plots are shown as supplementary material.

Discussion

The present study is to our knowledge the first to conduct association and prediction analysis with statistical methods tailored to handle competing risk data, in our case death as a competing risk to recurrence of CSDH. Our data shows that a considerable portion of patients (12%) dies during follow-up, which almost equals the risk of recurrence (14%).

Through this statistical approach, our association analysis gave rise to novel findings indicating that subdural drainage and longer drainage time seem favorable in the attempt to minimize risk of recurrence. Furthermore, we present two prediction models for future recurrences based on preoperative and postoperative variables. These models were translated into nomograms to provide clinicians with a tool to estimate the individual risk of recurrence of their patients.

Association analysis

Although the main focus of this study was to build a prediction model for recurrence, we included association analyses to compare our results with other studies. We found GCS, hematoma size, drain type, drainage time, and surgical complications to be significantly associated with time to recurrence. These findings are in accordance with previous studies [3, 12, 19, 23].

GCS is not a persistent risk factor of recurrence when reviewing the literature. The GCS is still most likely influenced by hematoma size depending on the degree of atrophy, since larger hematomas give rise to higher intracranial pressure resulting in decreasing GCS. The GCS may therefore be confounded by the hematoma size.

It is well established that postoperative drainage reduces the recurrence rate after burr hole evacuation of CSDH [19]. It is not clear, however, whether the placement of the drain should be subdural or subgaleal/subepicranial. While Kaliaperumal et al. found no difference in recurrence rate in their relatively small RCT comprising 50 patients [13], Sjåvik et al. found active subgaleal drainage to be superior to passive subdural drainage. The study did not have any data on passive subdural drainage (applied in this study) leaving no evidence for the superiority of passive subgaleal drainage to passive subdural drainage [22]. Our results indicate that passive subdural drainage is superior to passive subgaleal drainage in reducing the recurrence rate, shown by a significant difference in SHR between subgaleal drain placement and subdural drain placement.

Concerning drainage time, we found a decreasing recurrence rate with increasing drainage time. A small RCT with a total of 65 patients comparing 48 and 96 h of drainage found no difference in recurrence rate between the two groups; however, lower morbidity scores favored 48-h drainage time [11]. Longer drainage time has important implications in terms of mobilization regimes and length of hospital stay and is associated with complications such as thromboembolic events. The question of the optimal drainage time for CSDH patients needs further investigation, and we are currently performing a national randomized controlled trial comparing 24-h drainage with 48-h drainage.

We did not find any influence of anticoagulant or antithrombotic therapy on the time to recurrence. This is perhaps surprising, acknowledging that antithrombotic therapy is a major risk factor for the development of CSDH, but our results are in accordance with another recent Scandinavian study [7].

Predictive modeling

Our prediction model A found hematoma size, hematoma density, history of hypertension, drain type, drain time, and surgical complications as predictors of time to recurrence. In the penalized regression approach combined with stability selection applied in this article, variables were selected with a specific frequency. This frequency roughly reflected the importance of the variables in predicting recurrence in our dataset. Especially, hematoma size was the most important variable in predicting recurrence followed by the presence of complications, drain type and density, drain time, hypertension, and the remaining variables (shown in supplementary material).

When comparing our prediction model with the grading system for prediction of postoperative recurrence by Stanisic et al. [23], there are similarities in that both models predict high risks of recurrence with large hematoma size and separated hematoma densities. Our study did not include information about postoperative residual cavity volume, which makes it impossible to evaluate the performance of Stanisic's prediction model in our data.

A history of hypertension was found as predictor of recurrence in our models, but is to our knowledge not known as a risk factor of recurrence. It was not included in the prediction model from Stanisic et al., although it was included in their association analysis. The association between hypertension and recurrence is however plausible. Following the widely accepted hypothesis of CSDH growth due to micro bleeding from fragile neocapillaries [6, 20], an elevated pressure in the capillaries due to hypertension may increase the risk of these bleedings.

Our prediction models A (postoperative) and B (preoperative model) are illustrated in our nomograms (Fig. 3 a and b). A nomogram is a graphical way to calculate a patient's model-based predicted risk of recurrence on the basis of the cumulative score of all predictors in the model. The nomograms also illustrate how important each predictor is for the final risk assessment, e.g., a large hematoma size is correlated to high scores and thereby an increase in risk of recurrence, while hypertension has a small impact on the total cumulative score being 10 points if "yes" and 0 if "no."

Prediction vs. association

The prediction models are in accordance with our association model apart from including "history of hypertension" and "hematoma density". It is important to acknowledge that association models (also referred to as explanatory models in what follows) and prediction models are telling us two different things, although conflation between association and prediction models is common. In predictive modeling, as opposed to explanatory modeling, we do no longer seek after potentially causal connections, but aim at forecasting the time-dependent risk of recurrence for new observations based on the information contained in our variables. These two goals are different in nature and explanatory models are typically different from predictive models, as the latter exploit any kind of connections between the variables in the dataset, no matter which principles underlie, whereas explanatory models are often based on causality considerations (although causality can generally not be deduced from observational studies alone). Explanatory models might nevertheless be thought of as good candidates for prediction models, even considering that often the measured data does not accurately reflect the underlying constructs, which results in a gap between the explanatory variables' ability to explain and those to predict and the fact that prediction models deviate from explanatory models. For a more complete discussion of these aspects, we refer to [21].

Predictive performance

The performance of our model was evaluated at different points in time during the first 3 months following surgery. Our models appear to be reasonably well calibrated, that is, predicted risks correspond well to observed frequencies, but their discriminative performance is limited. Apparent c indexes were estimated to be approximately 0.67, and when corrected for the expected optimism in this estimate (because our model was trained and evaluated using the same data), we obtained a value of 0.63. The fact that a c index of 0.5 corresponds to random predictions (classifying patients into with or without recurrence by tossing a coin) whereas c indexes above 0.8 are considered good and a c index of 1 is perfect shows that although the variables in our prediction model do contain information that can be successfully exploited to predict the corresponding risk, correct classification into recurrence and non-recurrence is difficult due to the remaining randomness. This should be kept in mind, when transferring the predictions into clinical practice.

Our results correspond well to what was observed by Stanisic et al. [23], whose prediction model presented in their Table 4 achieved an apparent AUC of ca. 0.78, which can be assumed to be overly optimistic because of the same reasons. Their seemingly higher apparent AUC (0.78 vs. 0.67) might be due to pure chance (they evaluate in a dataset with only 17 recurrences) but also due to the fact that they have access to the postoperative residual cavity volume.

Conclusions

We found that a prediction model for time to recurrence of unilateral CSDH may be a valuable tool for individual risk assessment before and after surgery. The predictive performance indicates that factors that are still unknown or unaccounted for play a significant part in the pathophysiology of CSDH recurrence. We provide nomograms for easy assessment of the risk of recurrence.

The results of the association analysis as well as the prediction model suggest that size of the CSDH is the most consistent risk factor and predictor of recurrence, and that subdural drain placement is superior to subgaleal/subperiosteal placement. The association analysis points towards longer drainage time as a protective factor for recurrence. The optimal drainage time remains uncertain and further studies are needed to clarify this matter, ideally by an RCT.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval For this type of study, formal consent was not required.

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