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Predictive model for preoperative risk calculation of cerebrospinal fluid leak after resection of midline craniofacial mass lesions

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ABSTRACT

Background: Complex anterior skull base defects produced by resection of mass lesions vary in size and configuration and may be extensive. We analyzed the largest single-center series of midline craniofacial lesions extending intra- and extracranially. The study aims at the development of a predictive model for preoperative measurement of the risk of the postoperative cerebrospinal fluid (CSF) leak based on patients' characteristics and surgical plans.

Methods: 166 male and 149 female patients with mean age 40,5 years (1 year and – 81 years) operated for benign and tumor-like midline craniofacial mass lesions were retrospectively analyzed using logistic regression method (Ridge regression algorithm was selected). The overall CSF leak rate was 9.6%. The ROSE algorithm and 'glmnet' software suite in R were used to overcome the cohort's disbalance and avoid overtraining the model.

Results: The most influential modifiable negative predictor of the postoperative CSF leak was the use of extracranial and combined approaches. Use of transbasal approaches, gross total resection, utilization of one or two vascularized flaps for skull base reconstruction were the foremost modifiable predictors of a good outcome. Criterium of elevated risk was established at 50% with a specificity of the model as high as 0.83.

Conclusions: The performed study has allowed for identifying the most significant predictors of postoperative CSF leak and developing an effective formula to estimate the risk of this complication using data known for each patient. We believe that the suggested web-based online calculator can be helpful for decision making support in off-pattern clinical situations.

1. Introduction

Reconstruction of defects in anterior skull base surgery remains the most challenging, especially for the evolving endoscopic endonasal techniques. Failed skull base reconstruction has a significant impact on patient outcomes being associated with various severe and life-threatening complications.[1,2] In meningioma surgery (olfactory groove and tuberculum sellae) endoscopic approaches still produce a higher risk of postoperative nasal cerebrospinal fluid (CSF) leak than transcranial approaches.[3] Pedicled flaps such as the pericranial flap are the mainstay of anterior fossa floor reconstruction.[4] In the endoscopic endonasal surgery, with the advent of the vascularized septal mucoperiosteal flap by Hadad-Bassagasteguy[5] and other flaps such as lateral nasal wall flaps,[6] the safety of tumor resection in the light of CSF leak complications has significantly increased.[1,7–10]

Focusing on the lesions that penetrate the midline anterior skull base, a surgeon should picture the potential area of defects. Unilateral or bilateral defects of the frontal sinus, cribriform plate, ethmoid labyrinth, orbit, sphenoid sinus, and their different combinations may exist in this anatomical region. Moreover, large defects extending between the frontal sinus and optic apparatus in the sagittal plane and between the orbits in the coronal plane may be encountered. According to M.R. Patel

Abbreviations: AUC, Area Under the Curve; CSF, Cerebrospinal Fluid; ROC curve, eceiver Operating Characteristic curve.

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et al, the mean distance between foramen caecum and tuberculum sellae is 45,1 ± 4,1 mm, and between medial orbital walls at the levels of anterior and posterior ethmoidal arteries reaches 20,7 ± 4,7 and 24,7 ± 2,5 mm, respectively, and the intracranial orifices of the optic canals are 19,3 ± 2,5 apart, with the mean area of extensive penetrating anterior skull base defect equal to 10,24 cm^2 [11].

In this study, we analyzed the largest single-center series of benign lesions that extend both intra- and extracranially, hence their resection produces complex penetrating skull base defects, which may include critical structures of the skull base such as optic nerves, anterior half of the circle of Willis. Surgical management is a dilemma: incomplete resection to preserve the integrity of the skull base may impede local control. A radical approach inevitably leads to the challenge of watertight skull base reconstruction. Their management lacks guidelines due to the rarity of this type of pathology. This study aimed to suggest the instrument that would help estimate the risk of postoperative CSF leak in the given clinical situation based on the individual characteristics of patients and the surgical plan.

2. Materials and methods

Three hundred fourteen patients with benign and tumor-like midline craniofacial mass lesions were retrospectively analyzed using the logistic regression method. The series included a total of 314 patients (166 male and 149 female patients); age varied from 1 year and three months to 81 years (mean age was 40,5 years). All patients underwent surgical treatment in N.N. Burdenko National Medical Research Center for Neurosurgery, Moscow, Russia, between January 1st, 2001, and March 31st, 2018. Analyzed data were obtained from the primary surgery at the moment of patients' inclusion into the study; we considered all staged surgeries as combined interventions. Histologic types of lesions are presented in Table 1. All patients complied with inclusion criteria.

1. Clinical and radiological diagnosis of a tumor or tumor-like lesion (excluding meningocele and meningoencephalocele)
2. Histologically verified benign nature of the lesion
3. Primary or secondary midline anterior skull base localization
4. Intra- and extracranial extension
5. Formation of skull base defect in the central region of the anterior skull base (Fig. 1)

Outcomes of surgical treatment in terms of scientific challenge were measured by two options: noncomplicated postoperative course (absence of nasal CSF leak) and complicated postoperative course (presence of nasal CSF leak). Aim of the analysis was to evaluate the effects of selected factors (see the table in the Supplement) on the outcome and development of a formula for preoperative calculation of the probability of nasal CSF leak using baseline information (age, previous treatment, the extent of the lesion, localization and lateralization of skull base defect, type of defect, interactions of the lesion with skull base structures, extent of resection, surgical approach, and skull base reconstruction technique)..

A complicated postoperative course was observed in 30 observations. This number included any registered cases of CSF leak, including early (within 30 days after surgery) and/or occurred in the long-term follow-up. A relatively low frequency of CSF leaks led to the disbalance of the

Table 1
Histological types of lesions.

Group	Subgroup	Histological type	n
Meningioma			**125**
	WHO grade I		***112***
	WHO grade II		***13***
Nonmeningeal craniofacial lesions			**147**
	Nonmeningeal mesenchymal tumors		***43***
		Juvenile angiofibroma	15
		Hemangioma	10
		Ossifying fibroma	10
		Myofibroblastic tumor	2
		Angioleiomioma	1
		Myxoid fibroma	1
		Solitary fibrous tumor	1
		Fibroma	1
		Chondromesenchymal hamartoma	1
		Cementifying fibroma	1
	Osteogenic, chondrogenic, and odontogenic tumors		***58***
		Osteoma	39
		Osteoid osteoma	6
		Chondroma	6
		Osteoblastoma	3
		Chondromyxoid fibroma	3
		Ameloblastoma	1
	Bone tumors of undefined neoplastic nature		***33***
		Fibrous dysplasia	24
		Aneurysmal bone cyst	7
		Fibrous dysplasia + aneurysmal bone cyst	1
		Simple bone cyst	1
	Nerve sheath tumors		***7***
		Schwannoma	4
		Neurofibroma	3
	Epithelial tumors		***5***
		Inverted papilloma	4
		Adenoma	1
	Cysts and tumor-like lesions		***1***
		Epidermoid cyst	1
Inflammatory and infectious lesions with pseudotumor behavior			**42**
	Lesions with known etiopathogenesis		***41***
		Chronic rhinosinusitis with polyps	20
		Mucocele	19
		Non-invasive chronic fungal rhinosinusitis	1
		Wegener's granulomatosis	1
	Idiopathic lesions		***1***
		Granulomatosis of unknown nature	1
TOTAL			**314**

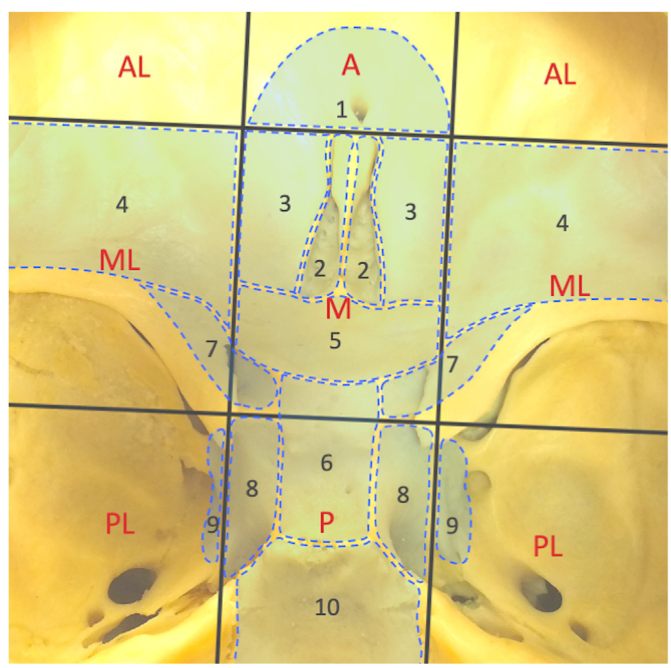

Fig. 1. Regions of anterior skull base involvement and schematic localizations of defects. A – anterior region, AL – anterolateral region, M– middle region, ML – mediolateral region, P – posterior region, PL – posterolateral region. Two sagittal planes correspond to the medial orbital wall, anterior coronal plane crosses the anterior margin of crista galli, posterior coronal plane crosses the anterior margin of tuberculum sellae. 1 – posterior wall of frontal sinus, 2 – olfactory fossa (with cribriform plate and lateral lamella), 3 – ethmoid roof, 4 – orbital roof, 5 – planum sphenoidale, 6 – sellar floor (with tuberculum sellae), 7 – optic canal, 8 – lateral sphenoid wall, 9 – lateral sphenoid recess, 10 – clivus.

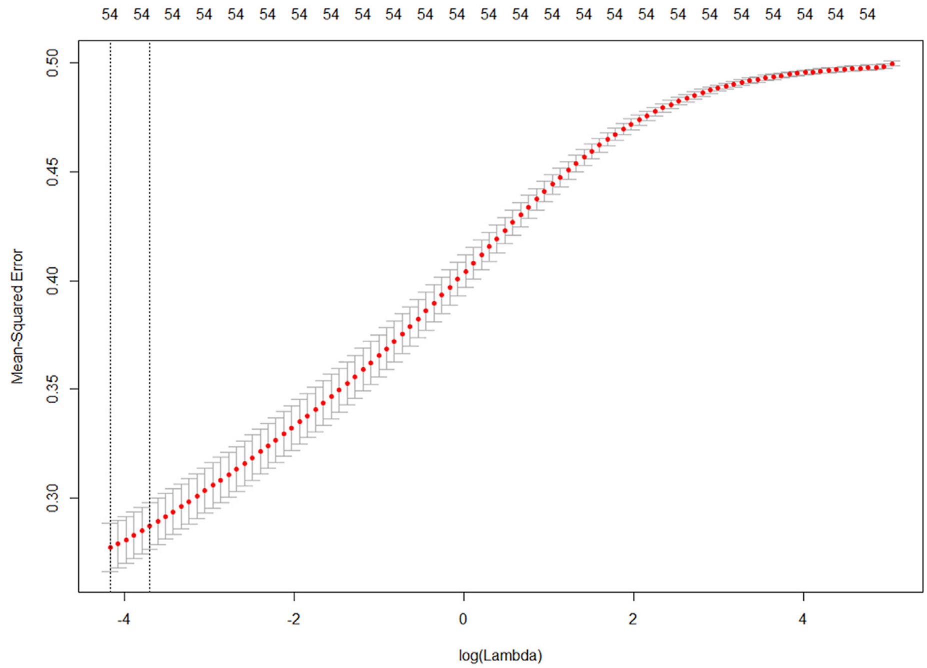

Fig. 2. Cross-validation of the model.

cohort. Hence the use of classical logistic regression would leak to prominently shifted evaluation of the probability of rare outcomes (9.6%). Therefore, we applied the ROSE algorithm in R by G. Menardi and N. Torelli, 2014[12], which creates a statistical matrix with balanced grouping based on analysis of conditional probability density of two classes in raw data. Due to an abundance of predictors int the model (see below) and risk of its overtraining, we used 'glmnet' software suite by J. Friedman et al, 2010[13] in R-Studio.

Two basic types of regularized logistic regression algorithms exist. Lasso regression (L1 regularization) is susceptible to zero weak predictors. It gives weight to strong ones, and ridge-regression (L2 regularization) is prone to decrease the weight of strong predictors and reveals weak predictors with low weight. Due to severe disproportion of positive and negative outcomes in the raw data, we selected a more liberal ridge-regression model to decrease model overtraining factors.

Cross-validation of the model with different values of regularization coefficient Lambda (number of folds = 10) is shown in Fig. 2. We selected a bigger value of Lambda (0.29), which corresponded to a statistically better model because this regularization parameter decreases the risks of model overtraining while preserving a low level of cross-validation error.

3. Results

3.1. Quality assurance of the model

We estimated how the probability of postoperative CSF rhinorrhea differed from the basic variable. Exponential coefficients exp(β) were implemented (Table 2). Quality control of predictions provided by the model required the use of raw data. Fig. 3 demonstrates the ROC-curve (Receiver Operating Characteristic curve) for the model of regularized logistic ridge-regression. The graph shows that the model reaches the accuracy of true-positive results of 50% at a frequency of false-positive results of 10% (cutoff point 0.7) and the accuracy of the true-positive results of 80% at a rate of false-positive results of 20%. ROC AUC (area under the ROC-curve) was 0.88 (compared to the generally accepted minimal value of 0.7 for biomedical studies).

Measures of quality of the model for different predictions of complication risk (negative outcome) are summarized in Table 3. It demonstrates that if criterium of a negative outcome is defined as 40%, then the number of false-negative results will be 3 (which comprised only 10% of the overall number of registered complications). However, in this case, the number of false-positive predictions is too high (approximately 29% of the total number of cases). On the contrary, if criterium of a negative outcome is defined as 70%, then the probability of false-negative results will be 16 (which represents approximately 53% of the overall number of registered complications), and the likelihood of false-positive predictions will be 26 (about 8%).

In surgical practice, the most severe risks are associated with false-positive predictions (which characterize the specificity of the model). It is recommended to use 50% as a criterium of probability.

3.2. Formula for calculation of probability of postoperative CSF leak

The formula for calculation of the probability of a negative outcome (P) is as follows:

$$P = \frac{exp(t)}{1 + exp(t)},$$

where $\boldsymbol{t} = -5{,}2 +$ [sum of category variables format (0 for absence, and coefficients of logistic regression (β) for presence]. The formula was actualized by the creation of the web-based online calculator, which is available via URL: https://denisgolbin.wixsite.com/calculator. It is made in the form of set of drop-down menus and checkboxes and immediately shows the result in per cent in the bottom.

To illustrate the use of formula, two randomly selected cases from the series are shown in Fig. 4. In case #115 (Fig. 4, upper section) estimated probability of postoperative CSF leak was 30%, which was considered as non-elevated. The postoperative course was uneventful. In case #169 (Fig. 4, lower section), the calculated probability of postoperative CSF leak was 70% indicating elevated risk. Her early postoperative course was complicated by CSF rhinorrhea, which required endoscopic defect reconstruction. However, in this patient with comorbidities, systemic complications eventually lead to a fatal outcome despite therapy.

Table 2
Effects of different variables of analyzed predictors on risk of postoperative nasal CSF leak.

#	Predictors	Variables	n	β	exp(β)
1	Age, years (basic variable – 0–10 years)	11–20	25	−1.49	0.23
		21–30	39	−0.70	0.50
		31–40	35	0.77	2.17
		41–50	61	1.07	2.90
		51–60	68	1.07	1.68
		61–70	36	0.36	1.43
		71–81	8	1.81	6.09
2	Previous treatment (basic variable – none)	Surgical only	126	0.67	1.95
		Radiation therapy	4	2.04	7.68
		Surgical and radiation therapy	9	0.00	1.00
3	Extent of lesion (basic variable – mostly intracranial extension)	Mostly extracranial extension	216	0.00	1.00
		Significant intra- and extracranial extension	61	−0.06	0.94
4	Regional skull base involvement (basic variable – none); see Fig. 1	Lateral region	256	1.55	4.72
		Anterior region	203	−0.11	0.89
		Middle region	312	1.02	2.78
		Posterior region	136	0.40	1.50
5	Localization of defect (basic variable – none); see Fig. 1	Posterior wall of frontal sinus	119	0.55	1.73
		Cribriform plate	97	0.10	1.11
		Lateral lamella	95	0.44	1.55
		Ethmoid roof	177	0.28	1.32
		Orbital roof	96	−0.25	0.78
		Medial orbital wall	130	0.15	1.16
		Planum sphenoidale	81	−0.85	0.43
		Sellar floor	31	−0.54	0.59
		Optic canal	24	0.40	1.49
		Lateral sphenoid wall	18	−1.88	0.15
		Lateral sphenoid recess	11	1.48	4.39
		Clivus	8	0.71	2.04
6	Number of localizations of defect (basic variable – 0)	1–12	253	0.02	1.02*
7	Lateralization of defect (basic variable – none)	Unilateral	136	0.00	1.00
		Bilateral	117	0.49	1.64
8	Type of defect (basic variable – none)	Bony	161	0.75	2.13
		Dural	3	0.57	1.78
		Penetrating (bony and dural)	89	0.81	2.26
9	Bony changes (basic variable – none	Hyperostosis	89	−0.22	0.80
		Destruction	220	−0.67	0.51
		Substitution by fibrous dysplasia	25	−2.25	0.11
10	Dural changes (basic variable – none)	Invasion	26	0.35	1.42
		Destruction	150	0.88	2.41
11	Involvement of critical neurovascular structures of the skull base (basic variable – none)	Contact	55	−0.29	0.75
		Invasion	30	0.33	1.38
12	Type of surgical approach (basic variable – suprabasal)	Transbasal	132	−0.77	0.46
		Subbasal	92	0.98	2.65
		Combined	49	1.12	3.05
13	Extent of resection (Basic variable – gross total resection)	Resection of intra- and extracranial portions of the lesion without	14	0.46	1.58
		transgressing the skull base	30	0.29	1.33
		Resection of intracranial portion	102	0.40	1.49
		Resection of extracranial portion			
14	Number of layers of reconstructive materials	1-4 (basic variable – 0)	168	0.34	1.41*
15	Quality of complex skull base reconstruction (basic variable – absence of vascularized flaps)	Only free non-vascularized flaps	19	0.18	1.20
		One vascularized flap	122	−0.28	0.76
		Two vascularized flaps	27	−0.66	0.52
		Three vascularized flaps	7	0.57	1.76
16	Perioperative CSF diversion via external lumbar drain	CSF diversion (basic variable – absence)	77	0.49	1.62
17	Intracranial hypertension (basic variable – absence)	Presence of intracranial hypertension	26	0.31	1.36

β – coefficients of regularized logistic ridge-regression, exp(β) – exponential coefficients of regularized logistic ridge-regression. * – explained in the text.

4. Discussion

4.1. Interpretation of obtained results

Age. Analysis of the effect of age on the risk of postoperative CSF leak showed that the younger the patient is, the lower is the probability of this complication. On the second decade the risk was higher (value of exponentiated coefficient '1.23' means that the risk is 1.23 times higher or increased by 23%; all values of exp(β) are read in the same way), and on the third decade, it was as twice as lower compared to patients of the first decade. On the contrary, in all age groups starting from 30 years, the risk was higher, especially in patients above 60, being eventually six times greater.

Previous treatment. Despite the type of treatment underwent before inclusion into the study, it increased the risk of postoperative CSF leak. However, considering few patients who received radiation therapy (a total of 13 with surgery or alone), the high value of the coefficient in the second group (risk was 7.68 times higher) should not be considered accurate as well as coefficient equal to 1 in the third group. The risk of CSF leak was two-fold higher in patients after previous surgeries.

Extent of lesions and involvement of skull base regions. Analysis of association between the risk of postoperative CSF leak and the extent of lesions showed no significant differences among the groups. Among analyzed skull base regions, all but anterior were negative predictors of postoperative CSF leak. Lateral extension increased the 4.72 times due to the high frequency of involvement of such critical structures as the optic nerve, cavernous sinus, or medial orbit.

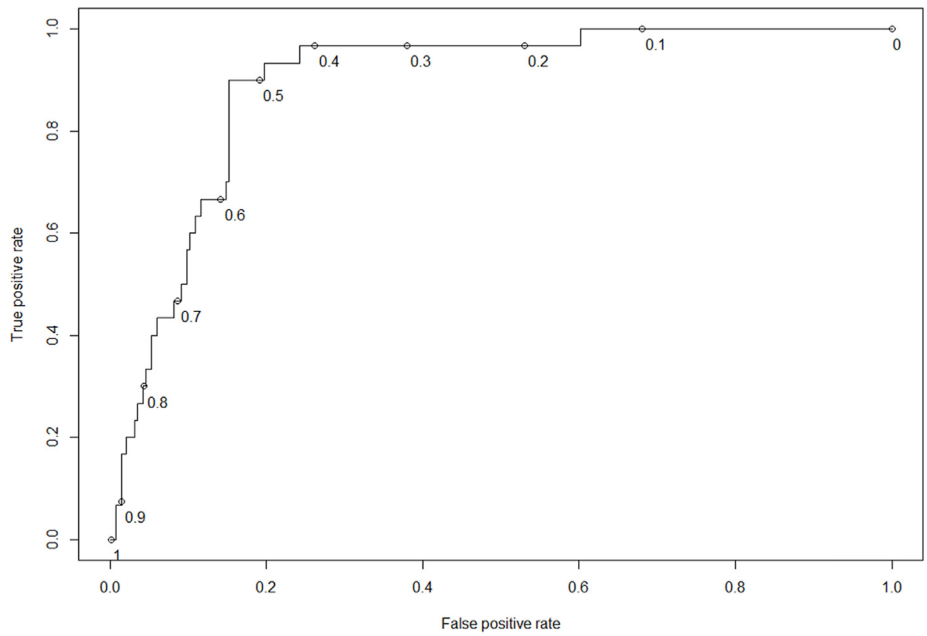

Fig. 3. ROC curve for regularized logistic ridge-regression model.

Table 3
Measures of quality of the model for different predictions of complication risk.

Parameters	Probabilities taken as negative outcome			
	40%	50%	60%	70%
Number of true-negative results	194	219	247	258
Number of false-negative results	3	5	11	16
Number of true-positive results	90	65	37	26
Number of false-positive results	27	25	19	14
Accuracy (95% CI)	0.70 (0.65–0.75)	0.78 (0.73–0.82)	0.85 (0.80–0.89)	0.87 (0.83–0.90)
Sensitivity	0.68	0.77	0.87	0.90

Sensitivity is defined as capability of the model to correctly identify positive cases (absence of complications). Specificity is defined as capability of the model to correctly identify negative cases (presence of complication).

Type, localization, lateralization, and number of defects. The presence of any defect negatively influenced the probability of postoperative CSF leak, provided that the most unfavorable type was penetrating (bony and dural) defect (coefficient was 2.26 against 2.13 in bony defect and 1.78 in dural). The relatively favorable effect of a purely dural defect was explained by the presence of underlying skull base hyperostosis and/or extracranial portion left unresected after removal of the intracranial portion of the lesion (13 of 16 cases).

Among localizations, the worse prognosis was in case of involvement of the following: the *posterior wall of the frontal sinus* (risk was 1.73 times higher), *lateral lamella* (1.55 times), *ethmoid roof* (1.32 times), *optic canal* (1.49 times) and in a lesser degree *medial orbital wall* (1.11 times) and *cribriform plate* (1.16 times). Herewith decreased risk of CSF leak was observed in case of involvement of the *orbital roof* (0.78), *planum sphenoidale* (0.43), *sellar floor* (0.59), and *lateral sphenoid wall* (0.15). It is explained by the following.

1) Perforation of the orbital wall is plugged by orbital fat;
2) Defects of planum are easily visualized and reconstructed;
3) Penetrating defects of the sellar floor and lateral sphenoid wall do not communicate with basal cisterns due to the pituitary gland and cavernous sinus; the transsphenoidal approach was applied in none of the cases.

Localization of defect in the *lateral sphenoid recess* (4.39) or *clivus* (2,04) was sparse (11 and 8 cases, respectively). Therefore, these numbers must not be considered accurate. With each additional localization, the risk of CSF leak was increased by 2%. I.e., in 1, 2, 3, 4, 5, 6, 7, and 12 localizations, the risk was increased by 2, 4, 6, 8, 10, 12, 14, and 24% (linear relation). Consequently, the maximal probability of CSF leak was 1,24 times. Unilateral defects did not impact the risk (coefficient was 1.00), and bilateral defects increased the risk by 64%.

Relations of lesions to the skull base structures. The presence of hyperostosis decreased the risk of CSF leak two-fold, and destruction – by 20%. Significantly lower risk (nine-fold) in the bone's substitution by fibrous dysplasia is consistent with its benign behavior. This type of lesion does tend to involve the dura (only 1 case of dural defect was detected and reconstructed). A non-aggressive approach to resection also plays a role (13 of 25 cases).

Analysis of dural changes showed that both invasion and destruction increase the risk of postoperative CSF leak (risk 1.42 and 2.41 higher, respectively). We suggest that the fixation of reconstructive tissues is technically more feasible in case of infiltrated dura than to disrupted; however, this may be debatable.

Contact between lesions and critical nerves and vessels without their invasion slightly decreased the risk of CSF leak (by 25%) while the invasion of these structured increased (risk was 1.38 times higher). In case of simple contact, the affected nerves and vessels are dissected off the lesion. Therefore, this situation is favorable. The presence of invasion of critical structures forced surgeons to leave these fragments of tumors unresected, and the possibility of proper fixation and adhesion of reconstructive tissues may be limited.

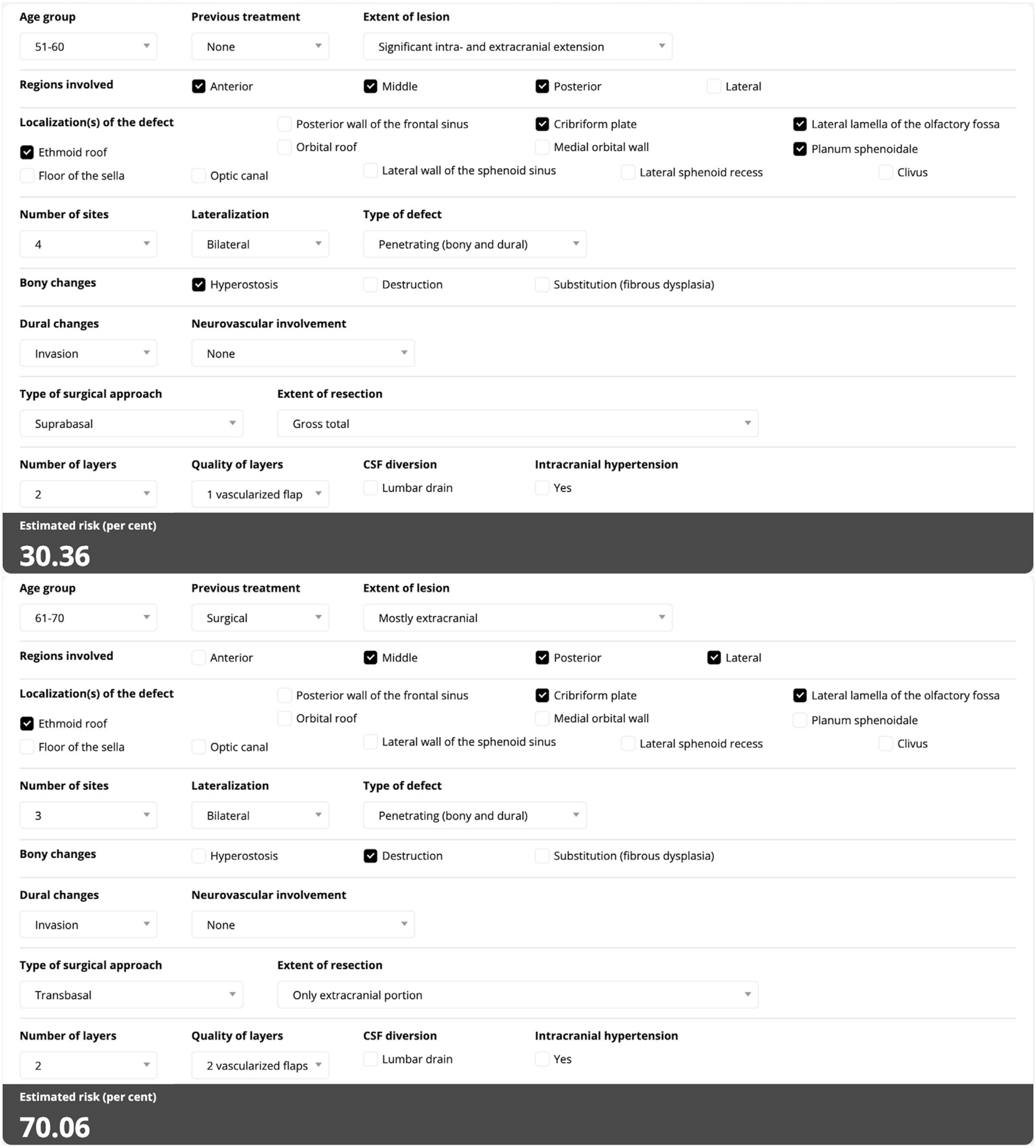

Fig. 4. Web-based online calculator for practical use of the formula. All variables with possible variants are included. Upper section: example case #115 demonstrates the use of the formula; the patient does not fall into the group of high risk (p value = 0,30 = 30%). Lower section: example case #169 falls into the group of high risk due to p value reaching 0,70 = 70%.

Surgical approaches and extent of resection. Different surgical approaches demonstrated various outcomes. To simplify the description of approaches, we applied classification by A. Di Ieva et al[14] Compared with suprabasal, transbasal approaches (usually, transsinusofrontal approach) decreased the risk of postoperative CSF leak (coefficient equal to 0,46), providing excellent exposure of intra- and extracranial space and decent visualization of the entire defect. In subbasal (mostly, endoscopic endonasal) and combined approaches, the risk of CSF leak was higher (2.65 и 3.05 times, respectively). A possible explanation is insufficient visualization of defects in purely endoscopic resection and wider extension of complicated lesions operated using the combined technique.

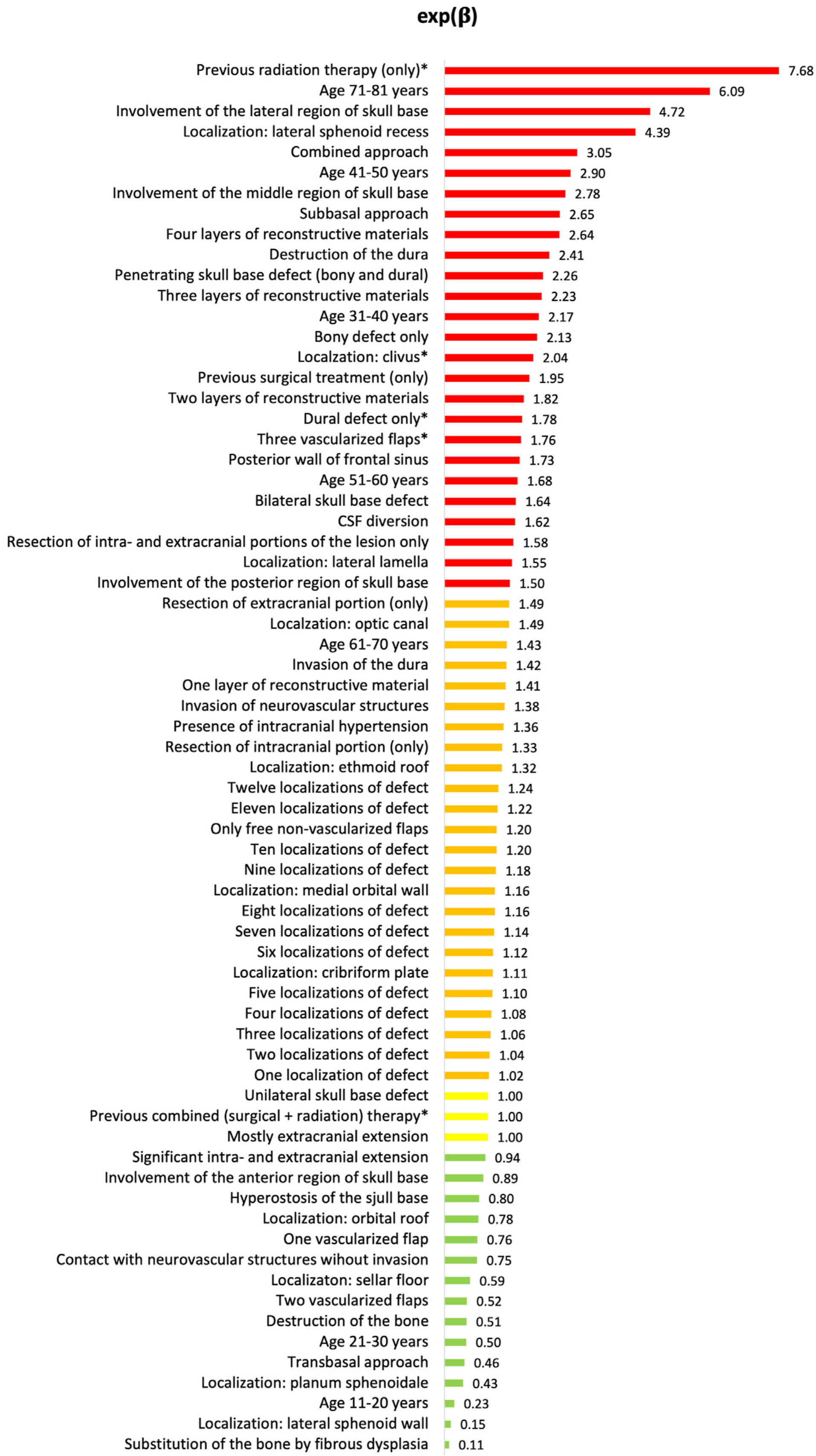

Fig. 5. Values of exp(β) listed in decreasing order. Red color: predictors with elevated risk by 50% and more; orange color: predictors with elevated risk by less than 50%; yellow color: neutral predictors (no elevation of risk); green color: decreased risk, * – unreliable values (with incidence less than 10 cases in the cohort).

Gross total resection was the most advantageous approach. Other types of incomplete resection moderately increased the risk of CSF leak by 33–58%. It should be considered that the resectability of lesions as well as area of skull base involvement depend on their size and extent. Lesions of smaller and moderate size were more frequently subject to gross total resection than large and giant. I.e., the significance of these coefficients is limited. Nevertheless, justified aim to radical resection is reasonable and safer due to better visualization of defects.

Qualitative and quantitative parameters of skull base reconstruction. An increase in the number of layers correlated with the risk of postoperative CSF leak. Each additional layer added 41%. Skull base reconstruction using 1, 2, 3, and 4 layers made the risk 1.41, 1.82, 2.23, and 2.64 times higher, respectively. It is explained by the monodirectional relation between the complexity of defects and the number of layers used for reconstruction. The more complicated the defect is, the more layers are employed for its closure, and the more difficult it is to achieve watertight reconstruction.

If only free non-vascularized flaps were used, the risk of CSF leak was increased by 20%. This association complies with numerous pieces of evidence for the superiority of vascularized flaps over free flaps. Using one or two vascularized layers decreased the risk by 24% and 48%, respectively. Reconstruction with three vascularized layers was associated with an increased probability of CSF leak (risk was 1.76 times higher). However, this represents the complexity of the defect.

CSF diversion and intracranial hypertension. Perioperative prophylactic CSF diversion using external lumbar drains was used in complex cases, and the coefficient 1.62 meant opting for this procedure in case of a substantial risk of reconstruction failure. Finally, elevated intracranial pressure added 36% to the risk of postoperative CSF leak.

The contribution of the present study to the problem of skull base reconstruction after tumor removal.

Skull base defect reconstruction and prevention of CSF leaks has always been one of the most significant challenges in surgery of the cranial base. Numerous techniques were proposed for watertight closure of anterior base defects after endoscopic, open, or combined tumor removal. They include local vascularized flaps, non-vascularized free flaps, less frequently used microvascular free flaps, and allogenic materials.[15–21] Prior studies have classified regions of the anterior cranial fossa for reconstruction, with a special respect to microvascular free tissue transfer.[22] Pedicled vascularized flap are superior to free flaps due to significant decrease of postoperative CSF leak rates even in patients who underwent radiation treatment and/or chemotherapy.[6,11,23,24] In one study, the meta-analysis with systematic review demonstrated no difference in the incidence of postoperative CSF leaks and meningitis after endoscopic anterior skull base surgery with reconstruction using autologous and non-autologous grafts.[25]

According to the literature, CSF leak prevention and prediction is best investigated in endoscopic endonasal transsphenoidal surgery due to large series and tremendous worldwide experience.[1,7,32–34,8,9,26–31] On the contrary, since the incidence of anterior skull base tumors with intra- and extracranial extensions is comparatively very low, evidence-based recommendations are limited in these pathologies.[10] It wound not be an overstatement to assert that surgeon's expertise and experience is of critical importance.[10,15,19,35]

Analysis of the literature data has demonstrated lack of similar studies. We found one published article, which is dealing with early and late complications after open and endoscopic neurosurgery for complex skull base and craniofacial pathology.[36] In this work, the incidence of CSF leaks was 13.3% in the series of 60 patients (compared with 9.6% in the present study). In some areas, our results are in concordance with the published data. For example, the presented analysis showed that the use of two vascularized flaps decreases the risk of CSF leak by almost 50%. Accordingly, the combination of vascularized pericranial flap with nasoseptal flap is a reasonable and efficacious option for prevention of CSF leaks in complex skull base reconstruction. This is consistent with other studies.[37,38] The number of anatomical localizations of the skull base defect was shown to be of little significance for anterior skull base defect reconstruction in cases of non-tumor CSF leaks.[39] In our study, each additional localization increased the risk of CSF leak only by 2% with the maximal value of 24% for all possible 12 localizations. It should be emphasized that we analyzed only benign lesions.

In our study, we have elucidated the most influential predictors of postoperative CSF leak (Fig. 5). However, only a few of them are modified predictors. The use of use of transbasal approaches (preferably transsinusofrontal approach), gross total resection, the inclusion of one or two vascularized flaps in the complex skull base reconstruction are the crucial examples of the surgeon's contribution to minimizing the risk of postoperative CSF leak.

The developed formula is a tool for calculation of the probability of postoperative CSF leak in percentage. Depending on this value, all patients are divided into two groups: with and without elevated risk of CSF leak. The level of 50% is a borderline between them. In this setting specificity of the model is as high as 0.83. Given that false-positive predictions (prognostic error in which the model indicates the absence of complication in case of its actual presence) pose the highest risks in surgery, these parameters of the model quality are the most practically oriented (see Table 3). If the probability of complication is 50% or higher, then elaborate preoperative planning is required, especially of the reconstructive step of the surgery and careful postoperative monitoring of the patient. Measures include a protective regimen, repeated nasal endoscopy, head CT scan in any doubtful situation, etc. Physicians should inform the patient and/or his caregivers about the aims of these procedures and the importance of compliance with the recommendations for the early postoperative period. The patient and/or his caregivers must be familiarized with the limitations to prevent elevation of intracranial pressure (open mouth sneezing, avoiding nose-blowing, and raising of weight over 7–8 kg, use of stool softeners when necessary[40]).

5. Conclusion

The performed study is based on the largest contemporary single-center series of anterior skull base lesions with intra- and extracranial extension. It has allowed for the identification of the most significant predictors of postoperative CSF leak and development of an effective formula to estimate the risk of this complication using data that are known for each patient. Modified predictors included the selection of approach (preferably transsinusofrontal), gross total resection, and the use of one or two vascularized flaps in the complex reconstruction of skull base defects. Possible practical applications of the suggested formula are not limited to predicting the risk of postoperative CSF rhinorrhea. Moreover, different surgical scenarios can be simulated using various options of modifiable predictors like surgical approach and components of skull base reconstruction. We believe that the suggested web-based online calculator can be helpful for decision making support in off-pattern clinical situations. It is available via URL: https://denisgolbin.wixsite.com/calculator.

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Credit author statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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