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ORIGINAL ARTICLE - NEUROSURGERY GENERAL

Bone resorption in autologous cryopreserved cranioplasty: quantitative evaluation, semiquantitative score and clinical significance

Lina Raffaella Barzaghi[1] · Veronica Parisi[1] · Carmen Rosaria Gigliotti[2] · Lodoviga Giudice[1] · Silvia Snider[1] · Antonio Dell'Acqua[3] · Antonella del Vecchio[2] · Pietro Mortini[1]

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Abstract

Background Changes after reimplantation of the autologous bone have been largely described. However, the rate and the extent of resorption in cranial grafts have not been clearly defined. Aim of our study is to evaluate the bone flap resorption (BFR) after cryopreservation.

Methods We retrospectively reviewed 27 patients, aged 18 years or older, subjected to cranioplasty (CP) adopting autologous cryopreserved flap. The BFR was derived from the percentage of decrease in flap volume (BFR%), comparing the first post-operative computed tomography (CT) and the last one available (performed at least 1 year after surgery). We also proposed a semiquantitative scoring system, based on CT, to define a clinically workable BFR classification.

Results After a mean ± SE follow-up of 32.5 ± 2.4 months, the bone flap volume decreased significantly ($p < 0.0001$). The mean BFR% was 31.7 ± 3.8% and correlated with CT-score ($p < 0.001$). Three BFR classes were described: *mild* (14.8% of cases) consisting in minimal bone remodelling, CT-score ≤ 6, mean BFR% = 3.5 ± 0.7%; *moderate* (51.9% of cases) corresponding to satisfactory cerebral protection, CT-score < 13, mean BFR% = 25.6 ± 2.2%; *severe* (33.3% of cases) consisting in loss of cerebral protection, CT-score ≥ 13, mean BFR% = 54.2 ± 3.9%. Females had higher BFR% than males ($p = 0.022$). BFR classes and new reconstructive surgery were not related ($p = 0.58$).

Conclusions BFR was moderate or severe in 85.2% of re-implanted cryopreserved flaps. The proposed CT-score is an easy and reproducible tool to define resorption extent.

Keywords Autologous bone cranioplasty · Aseptic bone flap resorption · Cryopreservation · Radiological evaluation

Abbreviations

BFR	Bone flap resorption
BFR%	Percentage of decrease in flap volume
CP	Cranioplasty
CT	Computed tomography
GOS-E	Extended–Glasgow Outcome Scale

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✉ Lina Raffaella Barzaghi
barzaghi.linaraffaella@hsr.it

1 Department of Neurosurgery and Gamma Knife Radiosurgery, IRCCS San Raffaele Scientific Institute, Vita-Salute University, Via Olgettina 60, 20132 Milan, Italy

2 Department of Medical Physics, IRCCS San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy

3 Department of Neurocritical Care, IRCCS San Raffaele Scientific Institute, Vita-Salute University, Milan, Italy

Introduction

The treatment of intracranial hypertension, in the care of traumatic brain injury, aneurysmal subarachnoid haemorrhage and ischemic stroke, may require decompressive craniectomy [1, 7, 11, 12, 26, 38]. After acute disease recovery, most patients undergo reconstruction of the cranial vault using autologous flap or a bone substitute to achieve cerebral protection, restore cosmesis, facilitate the rehabilitation and enhance neurological outcome [21]. Although various synthetic materials have been proposed, autologous bone flaps are widely used since they are relatively inexpensive, easily available, exhibit good fit and contour, present low risk of disease transmission or immunological reactions. They might, potentially, allow its incorporation through a remodelling process, achieved by vascular invasion, osteoclastic and osteoblastic ingrowth, resorption and osteogenesis [25, 29, 35, 36]. However, bone flap resorption (BFR) should be considered as a late complication, even though its incidence is considerably variable according to the criteria applied (clinical or radiological) [2, 4–6, 8–10, 13, 18, 21, 24, 25, 27, 28, 30, 32, 34, 37]. Currently, no official parameters for BFR definition are universally adopted since literature data are confusing. Indeed, some authors evaluate BFR as the need of new cranioplasty (CP) or revision surgery, while others define it according to a radiological feature [3, 4, 8, 9, 13, 14, 16, 17, 20, 21, 27, 28, 30, 34, 37].

The aim of the study is to describe the frequency, the entity and the clinical relevance of the BFR in autologous cryopreserved cranial flap. Our analysis is based on qualitative and quantitative changes of the graft, evaluated on long-term computed tomography (CT) scans after reimplantation.

Methods

Patient selection

Between September 2012 and April 2016, 67 patients submitted to decompressive craniectomy for intractable intracranial hypertension were treated at our institute. In all patients, autologous bone flap was cryopreserved. Among these, 18 patients died before CP or just several months after and are not included in this study. Exclusion criteria were as follows: (1) patients at surgery with age < 18 years (due to restricted use of CT scan in paediatric age according to radioprotection), 3 cases; (2) patients with less than 1 year of radiological follow-up, 19 cases. Finally, 27 cases are analysed.

Bone flap collection and storage

During craniectomy, the neurosurgeon performed three biopsies of the bone flap, and each biopsy was inoculated in a culture medium to evaluate the growth of aerobic, anaerobic and myceteal germ (Brain Heart-Schaedler-Sabouraud liquid modified–© Liofilchem ®, Teramo, Italy). The bone flaps were submerged in saline solution by the addition of antibiotic drugs (rifampin 90 mg/18 ml, Rifadin ®, Sanofi Aventis, Milano, Italy), packaged in double-wrapped sterile plastic (Nasco WHIRL-PAK ®, Milano, Italy) and stored in a non-sterile container (Nalgene™ Thermo Fisher Scientific, Waltham, MA, USA) at a temperature of – 80 °C; then, they were preserved at the Skeletal-Muscle Tissue Bank (Orthopaedic Institute, G. Pini, Milano, Italy). In the event of microbiological positive cultures, the bone flap was irradiated with 25 kGy at the Bone Bank of Bologna (Rizzoli Institute, Bologna, Italy).

Surgical procedure

Antibiotic prophylaxis (Cefazolin 1 g/4 ml, Cefazolina Teva, Milano, Italy) was intravenously administered before surgery. In the case of positive growth at culture, vancomycin was used: 1 g, 1 h before incision, administered as a slow intravenous bolus followed by 30 mg/kg/die for 72 h (Vancomicina Hikma, London, UK). The head was carefully shaved and the previous skin incision was reopened; the scalp flap and muscles were dissected from the dura and gently reflected. Once bone margins were fully exposed, the cryopreserved flap was positioned and secured using titanium plates and self-tapping screws. Multiple-layer wound closure over subgaleal drains was performed.

Clinical and radiological follow-up

The neurosurgeon assessed neurological status using the post-discharge structured interview for Extended–Glasgow Outcome Scale (GOS-E) at outpatient services or during phone interviews with the attending physician. Skin thinning and/or erosion, cranial irregularity or deformity as well as cranial pain were also considered. Radiological evaluation was performed comparing the first CT (done within 24 h after CP) with the last CT scan (performed at least 1 year after CP). All 27 patients underwent clinical and neuro-radiological evaluation at discharge and at follow-up evaluations.

Bone flap changes

The medical physicist calculated each bone flap volume with a Matlab code (Mathworks ®) after axial CT images segmentation with Medical Image Processing, Analysis and Visualisation (MIPAV software package version 7.20 National Institute of Health, Bethesda, MD, USA). The quantitative evaluation of BFR was derived from the percentage of decrease in volume of bone flaps, comparing the maximum volume (at the moment of implantation) and the minimum (at last follow-up), according to the following equation: BFR% = (volume at first CT − volume at last CT)/volume at first CT. Mean Hounsfield units (mHU) in the area of the bone flap and its variation in the last CT scan were also calculated in order to assess bone density.

The presence of selected radiological features of the bone flap was monitored by a neurosurgeon (qualitative analysis). Each feature when present was scored as reported in Table 1, assigning higher value to more evident and serious changes, as flap displacement or fragmentation, followed by peripheral or central bone loss, loss of differentiation between bone and diploe, jagged bone thinning, linear bone thinning and bone suffusion. Each of these features was scored with points, and the final semiquantitative CT-score was obtained from the sum of these points, on a scale from 0 to 18.

Table 1 Bone flap qualitative analysis based on last computed tomography (CT)

Radiological features	CT score (points according to presence/ absence of a radiolocal feature)	n	%
Bone suffusion	0.5/0	21/27	77.7
Linear bone thinning	1/0	18/27	66.6
Jagged bone thinning	1.5/0	15/27	55.5
Loss of differentiation between bone and diploe	2/0	20/27	74.1
Central bone loss	2.5/0	14/27	51.8
Peripheral bone loss	3/0	22/27	81.5
Fragment displacement	3.5/0	9/27	33.3
Flap displacement	4/0	15/27	55.5

Statistical analysis

All statistical analyses were performed using the IBM SPSS Statistics package (IBM Corporation, released 2011, SPSS Statistics for Macintosh, Version 20.0, Armonk, NY, USA). Continuous data were expressed as mean ± standard error and compared with the paired or unpaired Student's t test. The Anova test was applied for more than two group samples. Categorical variables were reported as number and/or percentage and were compared with the Pearson's chi-square with the Fisher exact test when appropriate. The Spearman correlation coefficient was used to correlate continuous variables. Multiple linear regressions were performed considering variables with p values < 0.01. The Cohen's k index was used to test the concordance between the two methods, semiquantitative and qualitative, adopted for resorption evaluation. The ROC analysis with the Youden criterion was used to define a cut-off value. P values < 0.05 were considered to be statistically significant.

Results

General results

Fifteen patients were female (55.6%) and 12 were male (44.4%). Mean age at CP time was 47.8 ± 13.6 years (range 20–73, median 50). The cause of intracranial hypertension was traumatic brain injury in 7 cases (25.9%) and vascular disease in 20 (74.1%) of whom 15 patients experienced haemorrhages (55.6%) and 5 ischemic strokes (18.5%), respectively. Twenty-six patients (96.3%) received a standard fronto-temporo-parietal decompressive craniectomy, and one patient (3.7%) underwent bilateral frontal decompression. In 14 cases (51.9%), a single flap positioning was performed, while in 13 (48.1%), the flap was fragmented in two or more pieces. Irradiation because of positive cultural test was dispensed in 6 cases (22%); *Propionibacterium acnes* was isolated in 5 cases (83%) and *Staphylococcus hominis* in one (17%). Eleven patients (40.7%) showed hydrocephalus at surgery: in 5 patients (45%), CP and ventriculo-peritoneal shunt were simultaneously performed; whereas, in the other 6 patients (55%) the shunt was positioned in a subsequent procedure. The mean cryopreservation time of the flap was 85.6 ± 10.2 days (range 23–217, median 65).

After a mean clinical follow-up of 33.5 ± 2.5 months (range 13–55, median 34), a statistical Glasgow Coma Scale improvement was seen as compared to that at discharge: GCS ≥ 10 in 23 patients (89.9%) vs. 17 patients (62.9%), respectively ($p < 0.001$). The GOS-E at last follow-up showed good recovery (grade 7 and 8) in 7 patients (25.9%), moderate disability (grade 5 and 6) in 3 patients (11.1%) and severe disability or vegetative state (grade 2, 3 and 4) in the remaining 17 (62.9%).

Early complications were observed in 2 patients (7.4%) who developed extra-parenchymal haemorrhages requiring surgical drainage. In one patient (3.7%), wound repair was necessary several months after CP because of skin dehiscence. Finally, a new heterologous CP was performed in 4 patients (14.8%), due to skin erosion associated with bone resorption in one case (3.7%) and for aesthetic issues in 3 cases (11.1%).

Quantitative analysis

After a mean radiological follow-up of 32.5 ± 2.4 months (range 12–54, median 34 months) bone flap volume significantly decreased (see Fig. 1; $p < 0.0001$). The mean value at surgery time was 56,460.2 ± 2765.2 mm^3 (range 21,016.5–90,326.2, median 56,460.2 mm^3) and 40,115.1 ± 3230.2 mm^3 at the last follow-up (range 12,611.5–70,988.2, median 39,708.8 mm^3). Mean BFR% was 31.7 ± 3.8% (range 1–74, median 31%) and did not significantly correlate with neither initial flap volume ($p = 0.41$) nor the mHU at first CT scan ($p = 0.92$).

The mHU evaluation demonstrated a significant modification from the first (1288.3 ± 46.6) to the last CT scan (1492.5 ± 62.1; $p = 0.011$), but this variation was not significantly related to the BFR% ($p = 0.64$).

Qualitative analysis

Table 1 reports data of qualitative analysis. The mean CT-score was 10.6 ± 0.8 (range 3.5–18, median 10.5), and it correlated significantly with the BFR% (Fig. 1; $p < 0.01$) but not with the mHU ($p = 0.39$). The Cohen's k index between CT-score and BFR% showed substantial agreement:

- CT-score ≤ 6 vs. BFR% ≤ 15% $k = 0.66$;
- CT-score ≥ 6.5 and < 13 vs. BFR% ≥ 16% and < 40%, $k = 0.78$;
- CT-score ≥ 13 vs. BFR% ≥ 40% $k = 0.69$.

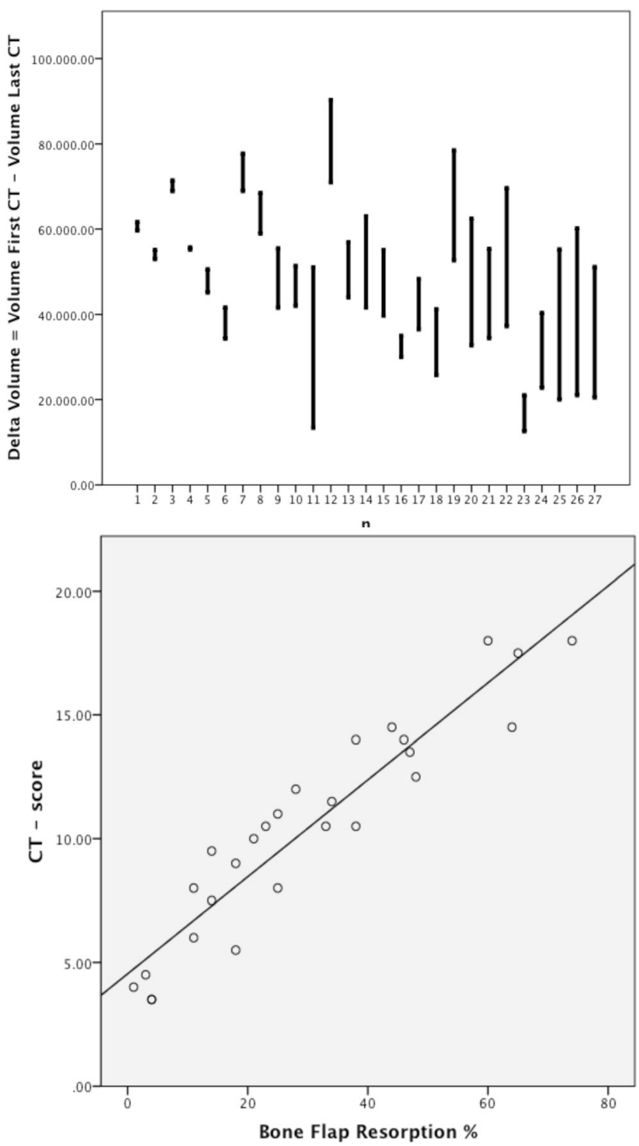

Fig. 1 Top: volume decrease during follow-up in 27 patients subjected to cranioplasty with cryopreserved autologous bone flap. Bottom: correlation between bone flap resorption (BFR%) and CT-score (Spearman correlation coefficient, $p < 0.001$)

Severity of bone resorption

We identified three classes of BFR, adopting the cut-off values of CT-score derived by ROC curves calculated on BFR%. A CT-score ≤ 6, corresponding to a volume decrease ≤ 15%, was considered the cut-off to define a *mild resorption*. In this grade, we observed fusion at CP margins with or without minimal evidence of bone resorption. A CT-score ≥ 13, calculated as volume decrease ≥ 40%, was the cut-off to divide moderate from severe resorption. *Moderate resorption* consisted in obvious bone reduction but with a satisfactory cerebral protection; whereas, *severe resorption* resulted in loss of cerebral protection (see Fig. 2).

Mild bone flap remodelling occurred in 4 patients (14.8%); the BFR was moderate in 14 (51.9%) and severe in 9 (33.3%), as showed in Table 2. In the *mild class*, no patients required surgery. In the *moderate class*, two patients were scheduled to repeat a surgical CP for aesthetic purposes or wound dehiscence, despite their low BFR% (30% and 35%, respectively) and their CT-score (8 and 10, respectively). In two severe cases, heterologous CP for both aesthetic and protective reasons was demanded; their BFR% was 46% and 74% and CT-score was 14 and 18, respectively. Conversely, all other 7 patients with severe resorption did not receive a new CP, because of either poor clinical recovery or surgery rejection (by themselves or their relatives). Based on quantitative and semi-quantitative analysis, any type or amount of BFR was recorded in all patients. However, only 4 patients (14.8%) underwent new surgery; indeed, both BFR% ($p = 0.12$) and CT-score class ($p = 0.58$) were not related with the replacement of heterologous CP.

Risk factors

Aetiology of decompressive craniectomy, bone flap fragmentation, ventricle-peritoneal shunt, irradiation nor the presence of medical comorbidity (smoke, dyslipidaemia) did not have any significant effect on resorption (Table 3). Despite age (≤ 30 years), poor clinical outcome (GOS-E ≤ 4) and cryopreservation time (> 2 months) seemed related with higher BFR%, only female gender ($p = 0.002$) and heart disease (0.048) were significantly related with resorption. The multiple logistic regression analysis confirmed the sex as risk factor for BFR ($p = 0.022$).

Discussion

Bone flap resorption: definitions, incidence, severity and clinical relevance

The BFR represents a late complication, occurring up to 1–2 years after autologous CP. The pathogenesis may be

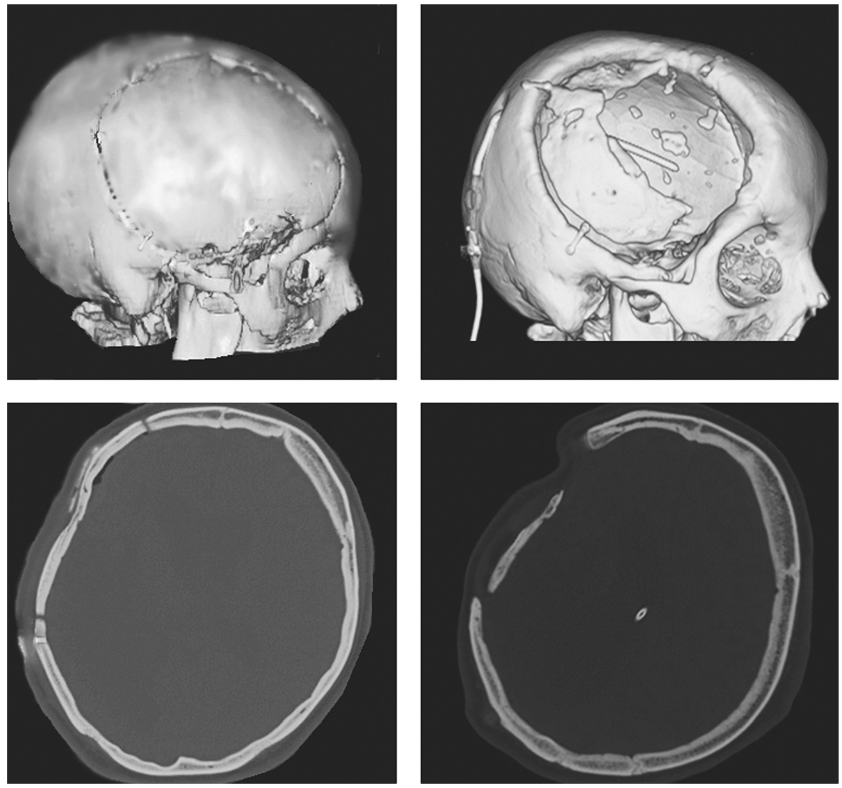

Fig. 2 Severe class of bone flap resorption: on the left, first postoperative CT scan, on the right, last CT available (performed 1.5 years after cranioplasty); 3D reconstruction above, axial section below

avascular necrosis or direct bone resorption by osteoclastic activity and enzymatic degradation of the collagenous matrix; therefore, the graft fails to reintegrate and adhere to the cranium, and the resulting instability does not favour the ossification; thus, a new CP may be required with additional morbidity [20, 33]. The incidence of BFR, defined as clinical palpable defect or implant loosening that necessitate reoperation, significantly varies from 1.4 to 32%. In the recent meta-analysis, the pooled rate was 20% [2, 4–6, 8–10, 13, 18, 21, 22, 24, 25, 27, 28, 30, 32, 34, 37].

When radiological parameters are considered for the definition of BFR, its incidence markedly rises up to 51–90.2% (see Table 4, supplementary material) [3, 4, 8, 9, 13, 14, 16, 21, 22, 27, 28, 30, 37]. Cheng et al. compared the thickness of the bone flap edge on operative side with the contralateral in a CT section passing bilaterally through the foramen of Monro; the BFR rate founded was about 30% [4]. Zhang et al. described three types of BFR with an overall rate of 46.3%: thinning (type I), reduced density (type II) and osteolysis within the flaps (type III); the incidence of moderate or severe BFR was higher in type III than in type I [37]. Stieglitz et al. reported 51% of BFR rate and proposed a score by summing the following parameters: thickness of bone (0–3), holes excluding temporo-basal gaps (0–1) and flap stability/dislocation (0–3); they advocated follow-up for patients with minor resorption and surgical revision for those with a score ≥ 6 [34]. Dunisch et al. classified a type I necrosis as a thinning of the bone flap and a type II necrosis as a complete lysis of the bone within the flap; the rate of BFR was 31.6% and 21.9% respectively and they considered type II necrosis to be an indication for surgical revision [8]. Finally, Korhonen et al., more recently, evaluated the radiologic bone flap volume, using the formula of the summation-of-area-method, and the radio density measured in Hounsfield units (HUs) [19]. Likewise our results, these authors comparing the initial volume with the last one during the follow-up described "*at least some BFR in 90.2% of the 41 selected patients;. … in contrast clinically significant BFR that required bone flap removal was found only in 4 patients (9.8%)*" [19].

In the current study, our first effort is to define the BFR after cryopreservation and to determine its frequency; thus, we used an objective and reproducible method (the measure of bone flap volumes on CT images) and we founded a mean BFR% of 31.7%. In all investigated cases, some resorption was observed. Subsequently, we combined the quantitative volume analysis with the qualitative CT data, calculating the semi-quantitative CT-score. Indeed, the measure of volume variation is objective but requires the CT scan obtained immediately after implantation, frequently not available [19], in addition to the last-one, and adequate software. The CT-score here proposed, even if might present certain grade of subjectivity, was calculated by a neurosurgeon blinded to quantitative analysis performed by a physicist, and it correlated well with the volume flap decrease (BFR%). This semi-quantitative score was based on qualitative radiologic data and estimates the volume changes with good concordance; it does

Table 2 Characteristics according to the classes of bone resorption

Bone resorption class CT score	Mild ≤ 6	Moderate < 13	Severe ≥ 13	*p*
n (%)	4 (14.8)	14 (51.9)	9 (33.3)	
Mean bone flap resorption (%)	3.5 ± 0.7	25.6 ± 2.2	54.2 ± 3.9	< 0.001
Mean CT score	3.9 ± 0.2	9.6 ± 0.4	15.2 ± 0.7	< 0.001
Re-operation: *n* (%)	0 (0)	2/14 (14.3)	2/9 (22.2)	0.580
Mean Hounsfield units on first CT	1254.1 ± 38	1313.1 ± 59	1265.1 ± 109	0.860

not require two CT-scans neither a dedicate software, therefore may be useful in the clinical practice.

Finally, in order to describe the clinical relevance of volume and bone changes, we divided the population in three classes of BFR severity: in our series, it was moderate (= evident bone loss but cerebral protection maintained, < 40%) in about half of cases and severe (= loss of cerebral protection, ≥ 40%) in one third, but only 4 patients (14.8%) required a new surgical procedure. In the authors' opinion, re-operation does not represent a realistic criterion to define the BFR since it underestimates its incidence. Otherwise, our results point out that BFR severity does not represent the only parameter for the indication to a second surgical procedure: skin thinning or erosion/dehiscence and especially neurological condition may be influencing factors that need to be considered. Patients with good neurological outcome may require new CP even in the presence of moderate BFR for aesthetic reason; whereas, in comatose patients, surgery represents an overtreatment even in the absence of bone protection because of their poor performance status. Thus, the relevance of BFR may be overestimated using radiologic criteria but underestimated by a strictly clinical empirical parameter (as re-operation). For this reason, we proposed a decision-making algorithm, that illustrates the management of patients treated with autologous cryopreserved CP considering the aforementioned CT-score, as estimation of BFR%, neurological and scalp conditions (see Fig. 3).

Risk factors associated with bone resorption

In our patients' cohort, we demonstrated for the first time that female gender represents a risk factor statistically associated with higher BFR%.

Several variables have been investigated in order to understand the mechanism underlying BFR (Table 5, supplementary material). Younger age is the most frequent risk factor reported in the published series: resorption is usually greater in patients aged ≤ 18 years, up to 66.7% [3, 8, 9, 14, 19, 23, 26, 30, 31]. Although young patients (≤ 30 years) had greater BFR% than older (> 30 years) also in our experience, statistical significance of the age as a risk factor was not confirmed, probably because paediatric population was ruled out from the present study, differently from others series (see Table 5) [3, 8, 9, 14, 19, 23, 26, 30, 31].

Table 3 Bone flap resorption and analysis of risk factors

	Volume decrease %, mean ± SE	Volume decrease %, mean ± SE	*t* test	Multiple linear regression
			p	*p*
Sex	Male, 19.3 ± 3.9	Female, 41.7 ± 4.9	0.002	0.022
Flap fragments	1 piece, 30.7 ± 5.7	2 or more pieces, 32.9 ± 5.3	0.781	
Flap irradiation	Yes, 26.3 ± 5.1	No, 33.3 ± 4.7	0.460	
Ventricular shunt	Yes, 31.9 ± 5.6	No, 31.7 ± 5.4	0.978	
Diabetes mellitus	Yes, 29.2 ± 6.7	No, 33.2 ± 4.8	0.648	
Heart disease	Yes, 15.6 ± 6.2	No, 33.3 ± 4.4	0.048	0.188
Dyslipidemia	Yes, 32.0 ± 4.6	No, 31.7 ± 4.3	0.984	
Smoke	No, 30.6 ± 5.6	Yes, 32.6 ± 5.3	0.811	
GOS-E	5–8, 22.6 ± 4.7	≤ 4, 37.2 ± 5.1	0.066	0.142
Pathology	TBI, 28.7 ± 7.4	No TBI, 32.8 ± 4.6	0.647	
Age	> 30 years, 30.6 ± 4.1	≤ 30 years, 38.5 ± 12.1	0.477	
Cryopreservation time	≤ 2 months, 26.0 ± 5.3	> 2 months, 36.4 ± 5.3	0.184	

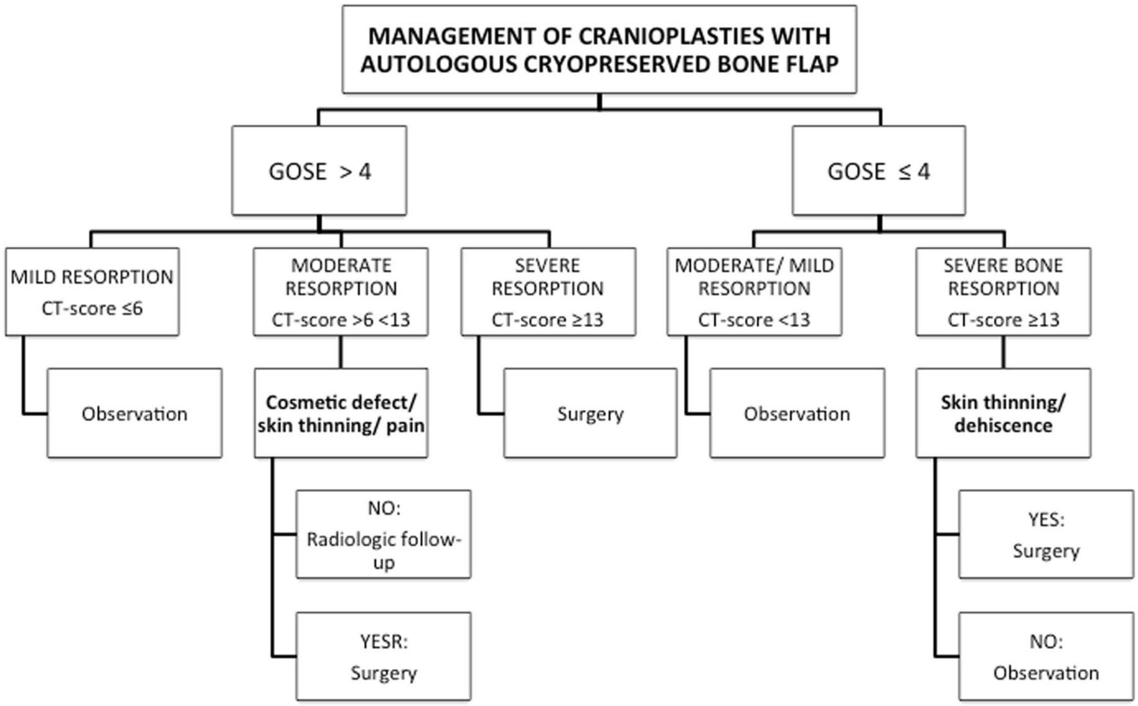

Fig. 3 Algorithm for clinical management in patients who underwent cranioplasty with cryopreserved autologous bone flap, according to the resorption classes (based on radiologic features, CT-score), Glasgow Outcome Scale–Extended (GOS-E) and clinical evaluation

Other risk factors for aseptic bone resorption reported in the literature are flap fragmentation [3, 4, 15, 22, 37] and presence of ventricular shunting [8, 22, 30]. BFR is more common in flaps with fractures because they may have fine local motion that promotes remodelling; indeed, reconstruction of skull defects using artificial materials is generally recommended when bone flaps are fragmented, but we did not find this association [3, 4, 15, 22, 37].

Additional risk factors which have been previously reported are: flap site [37], flap size (greater than 120cm^2) [9, 21], temporalis muscle resection [16], Glasgow Coma Scale at CP [15], unilateral CP [37], type of bone flap storage [4], duration of surgery (greater than 2 h) [13], traumatic brain injury [14], postoperative surgical site infection [30], postoperative wound dehiscence [8, 30] and prolonged cryopreservation period (> 12 months) [3, 9]. Regarding the cryopreservation, Stevenson et al. noted that it significantly reduces revascularization of the grafts and renders autologous bone flaps free of viable osteoblasts, but the Haversian systems and structural proteins remain intact regardless of its duration [33]. Therefore, a narrow contact between the flap and the recipient site associated with a rigid fixation shall ensure viable bone tissue by revascularization from the bony edges, periosteal layer and dura [3]. In our series, cryopreservation longer than 2 months seems to be related to higher BFR% even if statistical significance was not reached. It is of interest that irradiation, as processing of bone graft, did not increase the BFR%.

Limitations, interpretation and generalizability

The main limitation of this study is related to the retrospective and single-centre design as well as to the small cohort. However, despite these limitations, we were able to demonstrate that BFR occurred almost always in patients who have undergone CP with autologous cryopreserved flap, frequently without major clinical consequences, but in about one third of patients with loss of cerebral protection. The proposed CT-score may be helpful in the clinical practice because it is faster to perform as compared to the measure of flap volume variation. In consequence, the classification based on CT-score may be useful to assess the resorption extent and the protective function provided by the flap during the follow-up.

The risk profile of autologous CP still remains unclear, since literature data are not consistent [19, 20, 22]. Interestingly, we found female gender at risk of wide resorption, and we could speculate that the hormonal setting might play a role because both the subarachnoidal haemorrhage and the brain injury can damage the hypothalamus-pituitary axes. Unfortunately, we were not able to test the hormonal profiles of our patients, and therefore further studies, including long-term follow-up, are mandatory in this setting.

Finally, based on both recent published data [20, 22] and our results, primary heterologous CP may be considered: (1) in patients < 20 years, because children and adolescent present a different bone metabolism; (2) in patients with favourable neurological prognosis, since the risk of moderate BFR is about 50% and in these patients also cosmesis or pain for scar retraction may represent indications for reoperation. We suggest that age < 30 years, fragmented flap, shunting presence and long cryopreservation time alone do not influence the material choice, but may be considered in association with other risk factors when a neurosurgeon plans a CP to guarantee its success.

Conclusions

Based on our quantitative analysis, moderate and severe resorption occurred in 51.9% and 33.3% of patients, respectively, and in all population mean BFR% was 31.7 ± 3.8%. The long-term variation of flap volume between the first and the last CT scan correlated with qualitative radiological features at last follow-up, recorded as semiquantitative CT-score. Six or less points corresponded to mild resorption (< 15%); less than 13 points indicated moderate resorption with satisfactory cerebral protection (< 40%) and score equal to 13 or more meant severe resorption with cerebral protection loss (> 40%). Our semiquantitative score might be used to evaluate the severity of bone resorption and should be used in the decision-making process of second cranioplasty according to patients' characteristics during follow-up.

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Compliance with ethical standards

All procedures were performed in accordance with the World Medical Association Declaration of Helsinki and no submission to institutional ethical committee was required. Written informed consent was obtained by the patient itself or, in case of subjects unable to provide it, by next of kin.

Conflict of interest The authors declare that they have no competing interests.

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