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Pre-Implant Surgery
Meta Analysis

Harvesting anterior iliac crest or calvarial bone grafts to augment severely resorbed edentulous jaws: a systematic review and meta-analysis of patient-reported outcomes

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Abstract. The aim of this systematic review was to compare patient-reported outcomes after harvesting calvarial or anterior iliac crest bone grafts to repair severe jaw defects and enable implant placement. The MEDLINE, Embase, Cochrane Central Register of Controlled Trials databases, and OpenGrey were searched for studies on patient satisfaction, pain, disturbances in daily functioning, sensory alterations, donor site aesthetics, and complication rates. Of the 1946 articles identified, 43 reporting 40 studies fulfilled the inclusion criteria; the studies were one randomized controlled clinical trial, one retrospective controlled clinical trial, and 23 prospective and 15 retrospective cohort studies. A meta-analysis of two studies (74 patients) showed no difference in satisfaction (mean difference (MD) − 0.13, 95% confidence interval (CI) − 1.17 to 0.92; $P = 0.813$) or postoperative pain (directly postoperative: MD −2.32, 95% CI −5.20 to 0.55, $P = 0.113$; late postoperative: MD −0.01, 95% CI −0.14 to 0.11, $P = 0.825$) between donor sites. However, the level of evidence is limited, due to the retrospective, non-randomized design of one study. Postoperative gait disturbances were highly prevalent among the anterior iliac crest patients (28–100% after 1 week). The incidence rates of sensory disturbances and other complications were low, and the donor site aesthetic outcomes were favourable for both graft types. To conclude, harvesting bone grafts from the calvarium or anterior iliac crest to augment the severely resorbed edentulous jaw results in similar patient satisfaction. However, the findings for postoperative pain and disturbances in daily living suggest a trend in favour of calvarial bone grafts if harvested using an adjusted technique.

Keywords: Patient-reported outcomes; Bone grafting; Iliac crest bone; Calvarium; Alveolar ridge augmentation; Alveolar bone atrophy; Alveolar resorption; Partially edentulous jaw; Edentulous jaw; Treatment outcome; Dental implant.

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Autologous bone is considered the gold standard graft for compromised bone,[1,2] as it combines all of the required properties: osteoconduction, osteoinduction, and osteogenesis. Autologous bone is histocompatible and non-immunogenic. It is widely used in several surgical procedures for bony defect augmentation, including reconstruction of the mandible or maxilla to allow for reliable implant placement. For the repair of large defects, a frequently used and preferred donor site is the anterior part of the iliac crest.[1–4] However, the calvarial bone of the skull serves as a common alternative.[5–8]

As a donor site, the anterior iliac crest has several practical benefits: it is easily accessible and can provide ample amounts of cortical and cancellous bone.[2,5,7] Moreover, when using a two-team surgical approach, the harvesting can be done simultaneously with the augmentation surgery, thereby reducing the surgery time.[9] A common drawback of this procedure is the inherent donor site morbidity including pain, sensory alterations, and gait problems.[2] An alternative is the outer cortex of the posterior parietal skull bone. The calvarium provides ample amounts of cortical bone, but cancellous bone can also be obtained using a safe scraper.[10] Although the reports of morbidity following calvarial bone graft harvesting are promising,[5,11] the possibility of dura exposure or dura tearing are among the major arguments against calvarial bone grafting. Nevertheless, this risk has been minimized since the introduction of modified harvesting techniques.[5,10]

Regardless of the donor site, the related morbidity is a frequently mentioned drawback.[3,4] Some studies comparing anterior iliac crest and calvarial donor sites have indicated higher rates of minor complications following anterior iliac crest harvesting, such as postoperative pain, sensory alterations, and gait disturbances, and lower rates of severe complications after calvarial bone graft harvesting,[3,9,12] for example dural exposure. Therefore, the aim of this systematic review was to compare the patient-reported outcomes of harvesting from the calvarium and/or the anterior iliac crest to augment the maxilla and mandible with bone grafts. The morbidity and complications were also evaluated for these donor sites.

Methods

Protocol development

This systematic review was conducted following the recommendations of the *Cochrane Handbook for Systematic Reviews of Interventions* version 6.0. The reporting of this study complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement[13] and AMSTAR 2 (A MeaSurement Tool to Assess systematic Reviews; https://amstar.ca/index.php) to ensure quality and completeness. The study protocol has been registered in the PROSPERO database (International Prospective Register of Systematic Reviews; registration number CRD42021163926).

Information sources and search strategy

A thorough search of the literature was conducted with the help of a biomedical literature specialist; the search was completed on May 1, 2020 and updated on June 21, 2021. The primary database used was MEDLINE (via PubMed); Embase, the Cochrane Central Register of Controlled Trials, and OpenGrey were also searched. The search was supplemented by a hand-search of the references. Medical subject heading (MeSH) terms and free text words were combined in the search strategy according to the syntax rules of each database. Supplementary Material Table S1 depicts the strategy used in each database.

The following research question was formed: "Do patient-reported outcomes differ between patients treated with bone block grafts harvested from the calvarium and patients treated with bone block grafts harvested from the iliac crest, in the case of bone augmentation of the maxilla and/or mandible for dental implant placement?".

Consequently, the researchers based the literature search on the following PICO index: the population (P) comprised patients ≥ 18 years of age undergoing bone augmentation of the maxilla and/or mandible for dental implant placement; the intervention (I) was bone grafts harvested from the calvarium; the control (C) was bone grafts harvested from the anterior iliac crest; the outcome (O) was patient-reported outcomes (PROs). More specifically, the primary outcome was PROs in terms of general satisfaction (measured on a scale such as a visual analogue scale (VAS), or by means of a dichotomous question). Secondary outcomes were the severity (measured on a scale such as a VAS) and prevalence of postoperative pain assessed after 1 week, 1 month, 6 months, or > 6 months postoperatively; donor graft harvesting-related disturbances in daily functioning (i.e., difficulty when lying in bed, gait disturbances, headaches, difficulty with wearing clothes); sensory alterations (i.e., anaesthesia, hypoesthesia, hyperesthesia, or paraesthesia alongside the scar or due to injury of the lateral femoral cutaneous nerve); the aesthetic outcome at the donor site (i.e., patient satisfaction with donor site aesthetics), contour alterations, and abnormal scar formation; and the prevalence of major perioperative complications (i.e., bicortical harvesting of the iliac crest, fracture of the iliac crest, trepanation of the skull with or without dura tear, excessive haemorrhage) and minor perioperative complications (i.e. haematoma, infection, seroma, wound dehiscence).

The following inclusion criteria were applied: (1) randomized controlled clinical trials (RCTs), non-randomized controlled clinical trials (CCTs) with a minimum sample of 10 patients (five per group, or in the case of a split-mouth design at least five sites per group), and case series with more than five patients; (2) the repair of an extremely resorbed mandible and/or maxilla with bone block grafts from the calvarium or anterior iliac crest to optimize prosthetic function, or for the placement of dental implants; (3) detailed information available on PROs and procedure morbidities. No restriction was placed on language or year of publication. When necessary, a native speaker was asked to translate the title, abstract, or full text.

Exclusion criteria were (1) patients treated with bone grafts harvested from donor sites other than the calvarium or anterior iliac crest; (2) patients with known bone disorders or medical conditions that could affect the donor site

(parietal skull or anterior iliac crest); (3) systematic reviews, case reports, letters to the editor, expert opinions, conference abstracts.

Eligibility criteria

Two reviewers (D.E.W. and B.v.M) independently assessed the titles and abstracts identified in the initial search according to the inclusion and exclusion criteria. If the title and abstract provided limited information, or in the case of any doubt, the study was moved to the next round (full-text assessment). If a study compared anterior iliac crest or calvarial bone grafting with a control group not relevant to this review, such as a group treated with bone harvesting from other donor sites or treated with bone substitutes, it was assessed as a single-arm study. The results of the study assessments were compared, and Cohen's kappa (κ) and the percentage of agreement were calculated. Any disagreement was resolved through consensus. The full texts of the articles retained after title and abstract reading were assessed independently according to the eligibility criteria by the same observers. Cohen's κ and the percentage agreement were calculated, and any disagreement was resolved through consensus.

Risk of bias assessment

The risk of bias of RCTs was assessed using the Cochrane Collaboration Risk of Bias 2 (RoB 2) tool from the Cochrane Handbook for Systematic Reviews of Interventions version 6.0,[14] which assesses the following study-level aspects: (1) randomization (allocation sequence), (2) allocation concealment, (3) blinding, (4) completeness of outcome data, and (5) selective outcome reporting. This tool classifies studies into low, high, or unclear risk of bias.

The Newcastle–Ottawa Scale (NOS)[15] was used to assess the quality of the non-randomized studies (non-RCTs). Each study is judged on eight items, categorized into three groups: (1) selection of the study groups, (2) comparability of the groups, and (3) ascertainment of either the exposure or outcome of interest of the case–control or cohort studies, respectively.

Discrepancies between the two reviewers when assessing the quality of the included studies were resolved in a consensus meeting. A third reviewer (G.M.R.) was consulted to give a final judgment in the case a persistent disagreement. The percentage of agreement between the reviewers and Cohen's κ were calculated per item/domain of the tool used.

Data extraction

The data extraction was performed by the first reviewer (D.E.W.) using a predefined standardized form. A random sample of 30% of the extracted data was checked by the second reviewer (B.v.M.). Data on the study and patient characteristics, and the primary and secondary endpoints, were extracted. The method of assessment, moment of assessment (number of days or months postoperatively), and the outcomes were noted. If the moment of assessment varied among the studies regarding a certain outcome, the results were grouped by time frame (first week postoperatively, first month postoperatively, 6 months postoperatively, > 6 months postoperatively). If various rating scales were used for a continuous outcome, the scales were recalculated to a 0–10 score, with 0 representing the absence of the outcome ('no pain', or 'not satisfied') and 10 representing full presence of the outcome ('worst perceivable pain' or 'highly satisfied').

Statistical analysis

Inter-observer agreement was calculated using IBM SPSS Statistics version 20.0 (IBM Corp., Armonk, NY, USA). Data on the primary outcome (patient satisfaction) and secondary outcomes (intensity and prevalence of pain, problems in daily functioning, alterations of sensitivity, patient satisfaction with scar aesthetics, and prevalence of perioperative complications) were collected using Microsoft 365 Excel (version 16.50). The pooled mean difference (MD) and 95% confidence interval (CI) were calculated for the continuous variables, i.e. patient satisfaction and postoperative pain VAS scores, as these were the variables that were most comparable between the two distinct surgical sites. Statistical heterogeneity was regarded as substantial if $I^2 > 50\%$. The meta-analysis was performed using R package meta (version 3.5.3; R Foundation for Statistical Computing, Vienna, Austria), using a random-effects model because of clinical heterogeneity.

Results

Study identification and selection

A total of 3123 papers were identified. After excluding duplicates, 1946 papers were retrieved and screened by title and abstract (Fig. 1). Subsequently, 1870 papers were excluded (a list of all identified and excluded papers not presented in this review can be requested from the corresponding author). Disagreements (n = 64) were resolved in a consensus meeting. For the titles and abstracts screening, the percentage of agreement between the reviewers was 94% and Cohen's κ was 0.62. The full texts of the remaining 76 reports were screened and subsequently 43 reports were included.[16–58] Among these, three articles included data from studies described in other articles as well[17,18,30,31,34,35]; thus the data from both reports were combined. Finally, 40 studies were included for data collection and quality assessment (Fig. 1). The percentage of agreement was 91.4% and Cohen's κ was 0.82 for the full text assessment. Most studies reported data of just one of the arms and thus had no control group.

Assessment of methodological quality

A low risk of bias was seen in the following domains: 'deviations from intended interventions', 'measurement of the outcome', and 'selection of the reported results'. An intermediate risk of bias was seen in the domains 'randomization process' and 'bias due to missing outcome data'. A high risk of bias was observed in the 'selection of the groups' (69.2%). An unclear risk of bias was seen in 'exposure' (51.3%). The 'comparability of the groups' domain was only applicable to one retrospective comparative trial (Supplementary Material Table S2),[16] as the remaining studies had only one arm of interest for this review, and this was interpreted as a high risk of bias (97.4%). The Cohen's weighted κ was 1.0 for 'selection of the groups', 1.0 for 'comparability of the groups', and 0.88 for 'exposure'.

Study characteristics and interventions

The 40 included studies were one RCT, one CCT, 23 prospective cohort studies, and 15 retrospective cohort studies, published between 1993 and 2020 (Table 1). The follow-up ranged from 3 weeks to 228 months. Two studies declared funding from a research

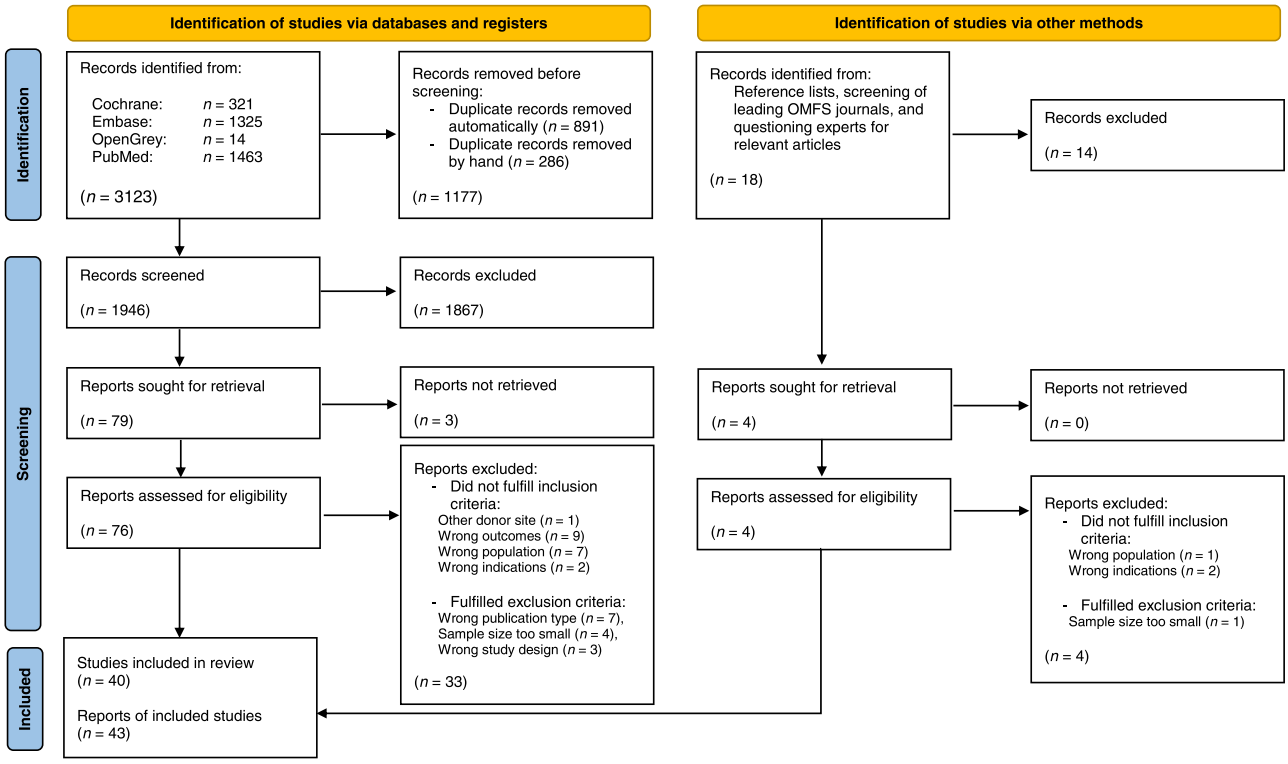

Fig. 1. Flowchart of the study identification and selection process.

programme[27,41] and 25 studies did not mention funding or conflict of interest.[16,19–21,23,24–26,28,29,33,36–38,40,42,44–46,49,50,51,53,54,59] All of the remaining studies declared that they did not have any funding or conflict of interest.

The techniques used for calvarial harvesting were similar to that described by Tessier,[59] Kellman,[60] and Schortinghuis.[5,10,16–18] The information on the prevention of intracranial perforations and filling of the contour defect varied. The calvarial defects were repaired by means of synthetic bone substitutes, such as polymethyl methacrylate (PMMA)[17,19,43] or titanium mesh or calcium phosphate cement.[54] The remaining studies did not repair the defect[33,37,44,55,56] or did not report information on a repair.[16,34,35,40] In one study, augmentation was combined with direct implant placement.[43]

Most of the anterior iliac crest monocortical blocks were harvested from the medial site.[18,20,21,24,27,29–32,36,38,41,45,48,49,55,57] Care for the lateral femoral cutaneous nerve, haemostasis, and the location of the incision was described in varying detail. Postoperative interventions, such as standard physical therapy and advice to use crutches, were only mentioned in 12 studies.[17,18,20,25,27,29,38,39,41,42,47,51,57]

Primary outcome: patient-reported satisfaction

Regarding the calvarial bone grafts, seven studies (206 patients in total) reported satisfaction with the procedure in general: the median VAS score ranged from 8.8 to 10[16,18]; 94–100% of the patients would recommend the procedure to others[16,18,33,44,55] and 90–100% would undergo the same procedure again if necessary[16,18,33,44,55,56] (Table 2).

Regarding the anterior iliac crest bone grafts, 13 studies (696 patients in total) reported general patient satisfaction: the median VAS score ranged from 9.5 to 10[16,18,31,48]; 92–100% of the patients would recommend the procedure to others[16,18,23,29,32,45,47] and 80–100% of the participants would be willing to undergo the same treatment again if necessary[16,18,22,23,28,29,31,32,45,48,53] (Table 2).

Secondary outcomes

Postoperative pain

Regarding pain severity, the reported median values for the highest pain experienced following calvarial harvesting, measured with a 0–10 VAS for all follow-up periods, ranged from 0.0 to 0.5,[16,18,33,40,43,56] with the exception of a median VAS score of 3.5 on day 2 postoperative reported in one study[18] (Table 2). For anterior iliac crest harvesting, the median pain VAS score during the first week ranged from 2.2 to 5.5[16,18,24,27–29,35] and then between 0.6 and 2.5 after 1 month.[18,25,29,36] The long-term median pain VAS score for both sites was 0.0[16,44] (Table 2).

The RCT revealed that the postoperative course of pain intensity was significantly higher for the anterior iliac crest graft patients compared to calvarial bone graft patients.[17] The comparative case series also demonstrated that early postoperative pain, assessed on recall, was significantly higher for the anterior iliac crest patients.[16] Furthermore, the RCT showed higher pain scores for patients with a higher body mass index (BMI) in the anterior iliac crest group, but not in the calvarium group.[18] With regard to pain prevalence, the two comparative studies reported equal outcomes for postoperative pain prevalence for the two sites: 20% during the first week[17] and 0%[16,17] after more than 6 months (Table 2).

Table 1. Characteristics of the included studies.

Author, year	Study design			Study population						
				Calvarium graft			Anterior iliac crest graft			Comorbidity[a]
	Follow-up (months)	Study type	Setting	*n*	Sex (%)	Age (years) Mean (range/SD)	*n*	Sex (%)	Age (years) Mean (range/SD)	
Comparative studies										
Kuik et al., 2016[16]	28.8[b]	CCT	MC	27	F: 48% M: 52%	60 (55–66)	27	F: 56% M: 44%	61.1 (55–67)	Unknown
Putters et al., 2018[17] (and Wortmann et al., 2019[18])	12[c]	RCT	SC	10	F: 50% M: 50%	65.9 (SD 8.7)	10	F: 60% M: 40%	63.5 (SD 7.0)	Excluded
Non-comparative prospective studies										
Raghoebar et al., 1993[19]	16[d]	PCS	SC	0	–	–	22	F: 48% M: 52%	48 (19–64)	Excluded
Chiapasco et al., 1999[20,e]	12[d]	PCS	SC	0	–	–	13	F: 78% M: 22%	42.1 (SD 12.5)	Excluded
Raghoebar et al., 1999[21]	32[d]	PCS	SC	0	–	–	65	F: 48% M: 52%	42 (SD 11)	Excluded
Stellingsma et al., 2003[22]	12[f]	PCS	SC	0	–	–	19	F: 83% M: 17%	59 (SD11)	Excluded
Joshi and Kostakis, 2004[23]	12[f]	PCS	SC	0	–	–	98	F: 62% M: 38%	44 (16–75)	Unknown
Nkenke et al., 2004[24]	1[c]	PCS	SC	0	–	–	25	F: 56% M: 44%	52 (SD 9.6)	Excluded
Weingart et al., 2005[25]	1[d]	PCS	SC	0	–	–	46	F: 56% M: 44%	55 (20–69)	Excluded
Gerressen et al., 2009[26]	5.2[d]	PCS	SC	0	–	–	15	F: 60% M: 40%	54.9 (39–72)	Unknown
Virnik et al., 2009[27]	8[b]	PCS	NR	0	–	–	20	F: 50% M: 50%	56.3 (43–62)	Excluded
Barone et al., 2011[28]	5[c]	PCS	SC	0	–	–	235	F: 66% M: 34%	54.3 (SD 10.2)	Excluded
Becker et al., 2011[29]	48[c]	PCS	SC	0	–	–	50	F: 48% M: 52%	52 (SD 2.0)	Excluded
Felice et al., 2011[30] (and Esposito et al., 2015[31])	12[c]	PCS	MC	0	–	–	13	F: 62% M: 38%	52 (29–65)	Excluded
Marianetti et al., 2013[32]	12[c]	PCS	SC	0	–	–	73	F: 59% M: 41%	49.3 (SD 14.55)	Excluded
Mertens et al., 2013[33]	28[d]	PCS	SC	12	F: 73% M: 27%	54 (30–71)	0	–	–	Excluded
Reissmann et al., 2013[34] (and Reissmann et al., 2018[35])	1[c]	PCS	SC	0	–	–	15	F: 60% M: 40%	46.1 (SD 15.5)	Excluded
Pistilli et al., 2014[36]	8[c]	PCS	MC	0	–	–	14	F: 50% M: 50%	49.5 (38–62)	Excluded
Sassano et al., 2014[37]	12[c]	PCS	SC	6	F: 67% M: 33%	63 (60–67)	0	–	–	Excluded
Fretwurst et al., 2015[38]	6[c]	PCS	SC	0	–	–	20	F: 75% M: 25%	54.3 (20–78)	Excluded
Putters et al., 2015[39]	25[d]	PCS	MC	36	F: 61% M: 39%	59 (SD 8.2)	0	–	–	Excluded
Mertens et al., 2017[40]	54[c]	PCS	SC	17	F: 94% M: 6%	54.3 (25–71)	0	–	–	Excluded
Cansiz et al., 2019[41]	0.75[c]	PCS	SC	0	–	–	10	F: 50% M: 50%	43 (SD 10.4)	Excluded
Elhadidi et al., 2019[42]	4[c]	PCS	SC	8	NR	NR	0	-	-	Included
Putters et al., 2019[43]	4[c]	PCS	SC	13	F: 69% M: 31%	68 (SD 9)	0	–	–	Excluded
Non-comparative retrospective studies										
Donovan et al., 1994[44]	31[d]	RCS	SC	24	F: 67% M: 33%	48 (20–67)	0	–	–	Unknown
Lundgren et al., 1997[45]	22[d]	RCS	SC	0	–	–	10	F: 90% M: 10%	55 (43–71)	Excluded
Kübler et al., 1999[46]	6[f]	RCS	SC	0	–	–	39	NR	NR	Excluded

Table 1. (*Continued*)

Author, year	Study design			Study population						
				Calvarium graft			Anterior iliac crest graft			Comorbidity[a]
	Follow-up (months)	Study type	Setting	*n*	Sex (%)	Age (years) Mean (range/SD)	*n*	Sex (%)	Age (years) Mean (range/SD)	
Cricchio et al., 2003[47]	24[c]	RCS	SC	0	–	–	70	F: 61% M: 39%	56 (38–69)	Unknown
Yerit et al., 2004[48]	144[d]	RCS	SC	0	–	–	28	F: 71% M: 29%	58 (SD 10)	Unknown
Barone et al., 2005[49]	5[c]	RCS	SC	0	–	–	18	F: 67% M: 33%	46.7 (37–60)	Excluded
Szabó et al., 2005[50]	6[f]	RCS	MC	0	–	–	20	F: 55% M: 45%	52 (28–67)	Excluded
Barone and Covani, 2007[51]	4.5[f]	RCS	SC	0	–	–	56	F: 68% M: 32%	NR (27–630	Excluded
Pelo et al., 2010[52]	44[c]	RCS	SC	0	–	–	19	F: 63% M: 37%	58.8 (48–68)	Excluded
Deppe et al., 2012[53]	6[c]	RCS	SC	0	–	–	54	F: 57% M: 43%	57.2 (NR)	Excluded
Restoy-Lozano et al., 2015[54]	45[d]	RCS	SC	11	F: 80% M: 20%	44 (R: 18–62)	0	–	–	Excluded
Quiles et al., 2015[55]	132[f]	RCS	SC	25	NR	NR	0	–	–	Unknown
Chiapasco et al., 2018[56]	228[d]	RCS	SC	72	F: 75% M: 25%	48 (R: 16–72)	0	–	–	Excluded
Sakkas et al., 2018[57]	24[f]	RCS	SC	0	–	–	38	NR	NR	Excluded
Gjerde et al., 2020[58]	94[d]	RCS	SC	0	–	–	44	F: 54% M: 46%	61.2 (SD 13.1)	Excluded

CCT, controlled clinical trial; F, female; M, male; MC, multicentre; NR, not reported; PCS, prospective cohort study; RCS, retrospective cohort study; RCT, randomized clinical trial; SC, single centre; SD, standard deviation;

[a]Comorbidity: patients with comorbidities affecting bone quality or quantity, or tissue healing capacity; or patients with pathological conditions at the donor site including previous surgery or irradiation of this area.

[b]Median follow-up period.

[c]Exact duration of the follow-up period.

[d]Mean follow-up period.

[e]This study included two patients treated with calvarium bone grafts who did not fit the review inclusion criteria, thus only the anterior iliac crest group was included.

[f]No information provided on the details of the follow-up data.

Disturbances in daily functioning and donor site sensory alterations

None of the calvarial bone graft harvesting patients reported disturbances in daily functioning after 6 months[16,17] (Supplementary Material Table S3). In the first week, the anterior iliac crest patients experienced gait disturbances, ranging from 28% to 100%,[20,24,29,32,38,45,47] and the necessity to use a walking aid which ranged from 11% to 100%.[23,28,36,38,46,51,52,58] This was temporary for most of the patients, but some studies reported that 4–20% of the patients had difficulties for more than 6 months[16,17,47] (Supplementary Material Table S3).

Neither of the comparative studies demonstrated a statistically significant difference regarding the prevalence of sensory alterations between the two donor sites[16,17] (Supplementary Material Table S3). Long-term objective sensory alterations following calvarial harvesting were seen in 0–15% of the patients.[16–18] Subjective hyperesthesia was reported in 7%[33] of the patients during the first week. Most sensory alterations following anterior iliac crest harvesting during the first postoperative week were reported as objective (0–52%)[23,24,28,38,46,47] and subjective (0–26%) hypoesthesia[23,24,26,28,38,46,47,50] (Supplementary Material Table S3). Paraesthesia was reported subjectively by 0–10% of the patients.[18,47,53,57] The long-term assessments demonstrated subjective sensory alterations in some cases (0–10%).[50,58]

Aesthetics at the donor site

Objective contour alterations were seen in 0–100% of the calvarial bone graft patients,[16,17,37,39,54] with the majority being subtle deficits[16,17,54] (Supplementary Material Table S4). Also, 0–85% of the patients mentioned contour alterations.[16,17,39] Scarring alopecia was reported by two studies, in 9% and 20% of the cases, respectively.[16,54] Regarding the anterior iliac crest grafts, objective contour alterations were seen in 3–67% of the patients,[16,17,47] even though only 1–19% of the patients reported alterations.[16,17,28].

The satisfaction score for the donor site aesthetics was high for both sites[16,29,32] (Supplementary Material Table S4). All the calvarium graft patients confirmed that they were satisfied with the donor site appearance,[16,18] while 60–100% of the anterior iliac crest participants were satisfied with the donor site aesthetics.[16,18,23,28,58] Younger patients were less satisfied with the aesthetics.[23] Regardless of the donor site, no patients considered the contour changes to be bothersome.[16]

Perioperative complications

With regard to the major complications, trepanation of the skull was an endpoint in seven studies. This comorbidity was

Table 2. Patient-reported satisfaction with the procedure (primary outcome) and postoperative pain (secondary outcome).

	Satisfaction with the procedure[a]							
	Rating, VAS (0–10) Mean (R/SD) or median (IQR)		Question–Satisfied? 'Yes' (%)		Question–Recommend? 'Yes' (%)		Question–Redo? 'Yes' (%)	
	Calvarium	AIC	Calvarium	AIC	Calvarium	AIC	Calvarium	AIC
Comparative studies								
Kuik et al., 2016[16]	10 (IQR 9.4–10)	10 (IQR 8.3–10)	–	–	96	96	100	89
Putters et al., 2018[17] (and Wortmann et al., 2019[18])	8.8 (IQR 8.1–10)	9.5 (IQR 9.0–9.5)	–	–	100	100	100	100
Non-comparative prospective studies								
Stellingsma et al., 2003[22]								90
Joshi and Kostakis, 2004[23]						92		85
Barone et al., 2011[28]								97
Becker et al., 2011[29]						95		80
Felice et al., 2011[30] (and Esposito et al., 2015[31])		10[b]						100
Marianetti et al., 2013[32]						97		100
Mertens et al., 2013[33]					100		100	
Putters et al., 2015[39]			95					
Non-comparative retrospective studies								
Donovan et al., 1994[44]					94		94	
Lundgren et al., 1997[45]						95		80
Cricchio et al., 2003[47]						94		
Yerit et al., 2004[48]		9.5 (R 8–10)						100
Deppe et al., 2012[53]								83
Quiles et al., 2015[55]			97		100		100	
Chiapasco et al., 2018[56]			90				90	
Gjerde et al., 2020[58]				85				

	Postoperative pain[c]								
	Severity Rating, VAS (0–10) Mean (R/SD) or median (IQR)		Timing (months)	Prevalence (%) 1st week		1 month		> 6 months	
	Calvarium	AIC		Calvarium	AIC	Calvarium	AIC	Calvarium	AIC
Comparative studies									
Kuik et al., 2016[16]	0.5 (IQR 0.0–3.0) 0.0 (IQR 0.1–0.0)	4.7 (IQR 2.4–8.0) 0.0 (IQR 0.0–0.0)	0.25[d] 27	–	–	–	–	0	0
Putters et al., 2018[17] (and Wortmann et al., 2019[18])	3.5 (IQR 1.0–5.0) 0.3 (IQR 0.0–1.0) 0.1 (IQR 0.0–0.1)	4.0 (IQR 2.0–4.0) 0.6 (IQR 0.2–2.1) 0.2 (IQR 0.1–0.3)	0.25[e] 1[d] 12	20	20	–	–	0	0
Non-comparative prospective studies									
Stellingsma et al., 2003[22]					85				
Joshi and Kostakis, 2004[23]					82		69		
Nkenke et al., 2004[24]		3.7 (SD 1.4)	0.25						
Weingart et al., 2005[25]		1.4 (SD 0.7)	1						
Virnik et al., 2009[27]		2.2[f]	0.25					0	
Barone et al., 2011[28]		5.5 (R 3–8) 3.3 (R 2–6)	0.25 0.5		99		64		0
Becker et al., 2011[29]		5[b] 2.5[b] 0[b]	0.25 1 12		48		36		0
Felice et al., 2011[30] (and Esposito et al., 2015[31])					100		100		0
Mertens et al., 2013[33]	0		12	0		0		0	

Table 2. (*Continued*)

Reissmann et al., 2013[34] (and Reissmann et al., 2018[35])		2.9 (SD 2.5)[g]	0.25		100		100			
Pistilli et al., 2014[36]		0.6 (SD 0.8)	1							
Sassano et al., 2014[37]				71						
Fretwurst et al., 2015[38]		NR[h]								
Putters et al., 2015[39]				100		25		0		
Mertens et al., 2017[40]	0		1	36		0		0		
Putters et al., 2019[43]	3.6 (R 20–70)		0.25	84						
Non-comparative retrospective studies										
Donovan et al., 1994[44]	0[b]		12	0		0		0		
Lundgren et al., 1997[45]					20		20		0	
Kübler et al., 1999[46]					5		5			
Cricchio et al., 2003[47]					86		43		0	
Barone et al., 2005[49]					22		0		0	
Barone and Covani, 2007[51]					11		0			
Deppe et al., 2012[53]					54		44		0	
Quiles et al., 2015[55]				19						
Chiapasco et al., 2018[56]	0.0 (IQR 0.0–4.0)		0.5							
Gjerde et al., 2020[58]		4.4 (SD 2.7)	NR		38		2			

AIC, anterior iliac crest; IQR, interquartile range; NR, not reported; R, range; SD, standard deviation; VAS, visual analogue scale.

[a]Results for patient-reported satisfaction with the procedure in general, assessed by means of a VAS score (with 0 representing not satisfied and 10 representing highly satisfied), and responses to a dichotomous question (yes/no) regarding whether they were satisfied, would recommend the treatment to others with a similar problem, and whether they would undergo the same treatment again if necessary.

[b]This study did not provide details on whether the value reported was the mean or median. Additionally, no SD, range, or IQR was provided.

[c]Results for the severity of postoperative pain, assessed by means of a VAS score (with 0 representing no pain and 10 representing the worst perceivable pain), with the corresponding timing of the assessment in months; the prevalence of pain at 1 week, 1 month, and > 6 months is also reported.

[d]Postoperative pain was assessed directly after harvesting on recall, and at follow-up 2.5 years later.

[e]In this study, the maximum pain scores were seen on days 2 and 3.

[f]This study reported that the use of additional pain medication was not necessary in any patient; other reports on pain or the use of medication were not provided.

[g]This represents the maximum pain felt during the first week.

[h]The pain that occurred in the patients was well controlled with non-steroidal analgesics.

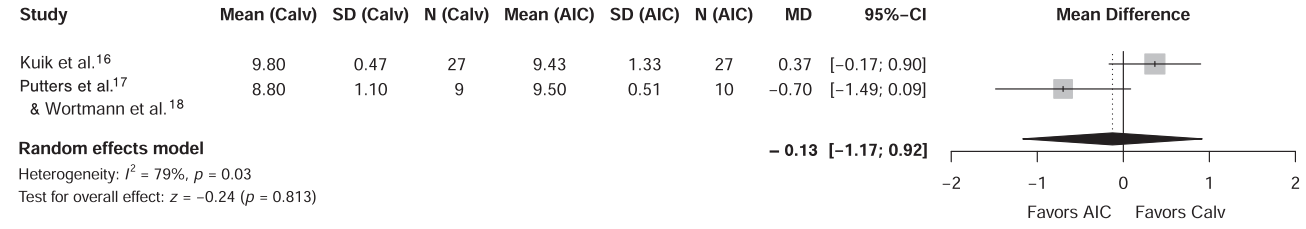

Fig. 2. Forest plot for pooled patient-reported satisfaction after harvesting calvarium versus anterior iliac crest grafts. Abbreviations: Calv: patients treated with calvarium grafts; AIC: patients treated with anterior iliac crest grafts; MD: mean difference; CI: confidence interval.

not seen in five of these studies,[17,33,37,40,56] but the remaining two studies reported an incidence of 11%[16,39] (Supplementary Material Table S4). After finding an incidence of 11%, Putters et al.[39] changed the harvesting technique during the study, whereupon this complication no longer occurred. All of the defects were closed immediately and healed without consequences in all cases. The incidence of anterior iliac crest fractures was 0–5%.[16,17,23,24,26,28,29,38,47] All of the fractures were treated conservatively and healed without further consequences. The minor complications among the participants treated with calvarial bone grafts or anterior iliac crest grafts are reported in Supplementary Material Table S4.

Meta-analysis

Data derived from the two comparative studies (two distinct patient populations) showed that the satisfaction of the patients with the procedure in general varied a lot (I^2 = 79%, P = 0.03), but the differences in VAS scores between the calvarial and anterior iliac crest harvesting groups were not statistically significant (MD −0.13, 95% CI −1.17–0.92; z = −0.24, P = 0.813) (Fig. 2).[16,18] The variation could be explained by the difference in timing of the assessment (12 and 27 months, respectively). No further subgroup or meta-regression analysis could be performed due to the small number of included studies.

A meta-analysis of the data derived from the two comparative studies with

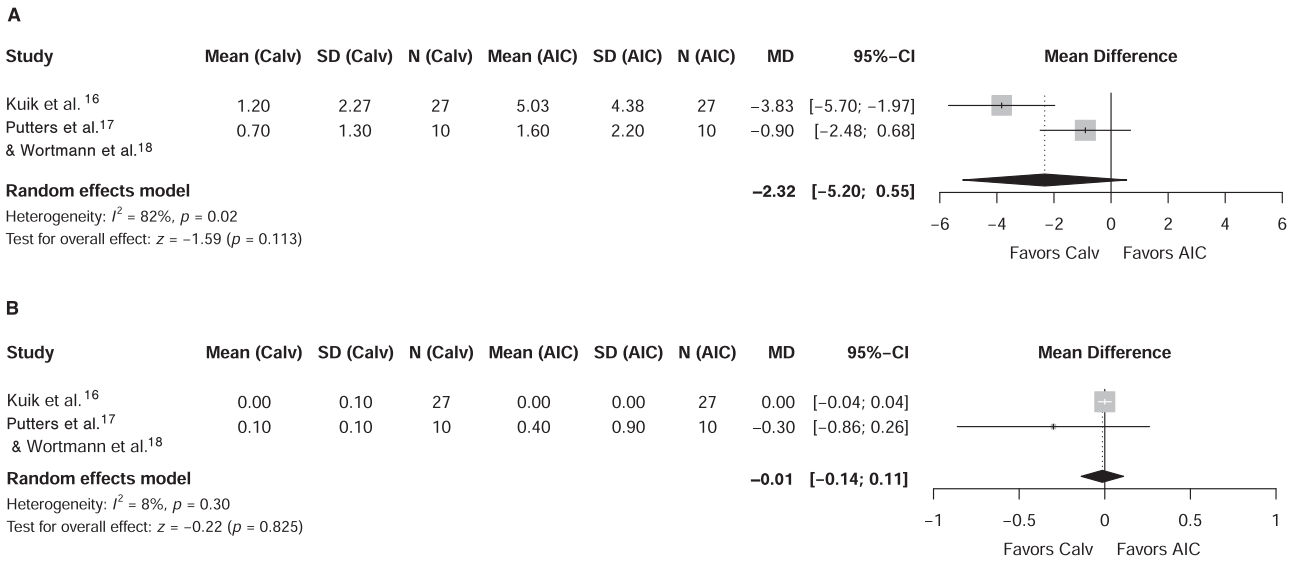

Fig. 3. Forest plots for the secondary endpoint—pooled patient-reported severity of postoperative pain after harvesting calvarium versus anterior iliac crest grafts: (A) immediately postoperative; (B) late postoperative. Abbreviations: Calv: patients treated with calvarium grafts; AIC: patients treated with anterior iliac crest grafts; MD: mean difference; CI: confidence interval.

two distinct patient populations resulted in a large variation in outcome with regard to the severity of pain immediately postoperative (I^2 = 82%, P = 0.02).[16,18] The VAS score for the direct postoperative pain outcome was slightly lower following calvarial bone harvesting, although the difference was not significant (MD −2.32, 95% CI −5.20 to 0.55; z = −1.59, P = 0.113) (Fig. 3A). Despite the late postoperative pain outcomes varying greatly as well (I^2 = 8%, P = 0.30), the difference in the VAS scores was not significant (MD −0.01, 95% CI −0.14 to 0.11; z = −0.22, P = 0.825) (Fig. 3B). The variations could be explained again by differences in the timing of the assessment (12 and 27 months, respectively). No subgroup or meta-regression analysis could be performed due to the small number of included studies.

Quality of evidence

All of the included studies had a high risk of bias due to the nature of the comparison: the surgeons and patients could not be blinded to the donor site used. Furthermore, only two studies were comparative. The quality of the evidence was moderate for patient satisfaction and postoperative pain severity according to GRADE.[61–63] The evidence for the remaining outcomes was of limited quality due to the high variations in outcome measures, the indirectness of the assessments, and due to data imprecision. The data derived from the prospective and retrospective cohort studies were assessed as being very low quality. Endpoints based on very low quality evidence cannot be used to make recommendations to surgeons and should therefore be interpreted with caution.

Discussion

This systematic review evaluated patient satisfaction, morbidity, and complications associated with anterior iliac crest or calvarial bone graft harvesting for dental implant placement. The meta-analysis showed that patient-reported satisfaction after undergoing calvarial bone graft and anterior iliac crest graft harvesting was similar. Furthermore, postoperative pain, sensory disturbances, and complications were limited and the donor site aesthetics ratings were generally very positive regardless of the donor site. However, based on both the comparative and non-comparative studies, the prevalence of daily disturbances seemed higher following anterior iliac crest harvesting.

The comparative studies demonstrated high patient satisfaction regardless of the donor site. Similarly, Falkensammer et al.[64] assessed patient satisfaction with anterior iliac crest harvesting for sinus lifting or onlay bone reconstructions in partially edentulous patients, and reported high acceptance as well; 84% of the patients would agree to undergo the same treatment if they had to choose, and 87% would recommend this treatment to other patients.[64] It appears that no other data on patient satisfaction following calvarial bone grafting exist.

Several possible factors affecting patient satisfaction could be identified from the literature. An important determinant of patient satisfaction is fulfilment of patient expectations, i.e. adequate information provided by health care providers can enhance patient appreciation.[65,66] Additionally, there is evidence that patient socio-demographic factors, e.g. education level, cultural background, and social network, can affect their satisfaction with the health services.[65] RCTs in the future could limit bias due to health service characteristics and socio-demographic factors. Also, in patients who underwent bone grafting surgery as part of a larger treatment procedure and improvements in denture function, any dissatisfaction with the harvesting surgery might have been overridden. Furthermore, patient-reported experiences are important predictors of overall patient satisfaction.[64,66] For example, postoperative pain, disturbances in daily living, or unfavourable scar formation may affect patient appreciation of the procedure.

In concordance with reports on calvarial and anterior iliac crest bone harvesting for other indications,[7,9,12,64] early postoperative pain was more evident after harvesting anterior iliac crest

bone. Several reports on the causes of pain following anterior iliac crest harvesting have suggested making technical adjustments to limit pain. These include minimizing the manipulation of the abductors from the ilium, avoiding nerve injury as well as using bone wax or other haemostatic materials to treat the cortices, and post-harvest reconstruction of the iliac crest.[2,67] There are also suggestions related to using a bupivacaine pump, but the evidence of the impact on morbidity is conflicting.[2,68] In the present study, an evaluation of the various harvesting techniques used for anterior iliac crest bone graft harvesting was not feasible as there was a lack of documentation of the exact harvesting method in most of the studies reviewed.

When choosing between the calvarium and anterior iliac crest, pain should be considered, particularly for patients with a higher a priori risk of elevated postsurgical pain. Specifically, the severity and duration of pain appear to be higher in patients who are younger, female, have a smoking habit, history of depressive symptoms, anxiety symptoms or difficulties, previous preoperative pain, and the use of preoperative analgesia.[69–72] However, some of the currently reviewed studies reported no correlations between pain and age or sex.[18,38] Additionally, in concordance with some of the currently reviewed studies,[18,38] a higher BMI has been associated with pain[69–73] and postoperative adverse events.[74,75] This may be due to compromised wound healing[76] or limited accessibility of the donor site, thereby strengthening the postoperative pain and gait disturbances following a manipulation of the tendo-musculoskeletal structures around the donor site.

The second most reported morbidity following anterior iliac crest harvesting is acute gait disturbance and chronic walking difficulties. This corresponds to a previous review.[67] It is postulated that gluteal stripping and subsequent postoperative pain is a major cause of gait modification following iliac crest bone harvesting.[2,64,67] Thus, the prevalence of pain and gait disturbances is expected to exhibit a similar course.

Acute sensory disturbances occurred in up to half of the patients whose anterior iliac crest was harvested and these were considered to be mostly objective alterations. Chronic sensory disturbances were not reported, in contrast to other reviews that have included patients undergoing spinal or orthopaedic surgery.[2,3,67] Their outcomes may have resulted from technical differences in harvesting surgery or differences in the required volume of grafted bone, since most sensory disturbances are believed to result from direct trauma or stretching injury of the lateral cutaneous nerve during anterior iliac crest harvesting.[2,3,67] Regarding calvarial harvesting, sensory alterations are attributed to a coronal incision or use of electrocautery.[7,77,78] A parasagittal incision and limited use of electrocautery is therefore advised.

Irrespective of the harvesting location, the patients were generally satisfied with the donor site aesthetic outcomes. Scalp contour alterations were not reported as causing dissatisfaction, probably because these alterations were covered with hair and most of the deficits were subtle. The appreciation of the aesthetics following iliac crest harvesting was lower in some studies. Patient expectations of the outcomes could play a role here, as patients might be more prepared for scar formation or contour alterations when calvarial bone is harvested. Since only two comparative studies were included, the identification of factors affecting satisfaction such as age, sex, and treatment necessity, could not be performed. Still, it is assumed that the skull is more at risk of significant aesthetic sequelae since it is part of a person's appearance, particularly since the donor site is located more superficially and hair becomes thinner with age. Therefore, contour alterations and alopecia associated with calvarial harvesting should be minimized.

Depression of the skull following calvarial harvesting is common.[7,77] It is explained by the incapacity of the periosteum to reproduce bone tissue of the same magnitude to refill the newly formed defect, in particular for defects larger than 2 cm.[2,79–81] Also, skull deficits are easily detected due to the superficial position. To minimize this, defects should be restored with a biomaterial.[82] Osteoconductive biomaterials that undergo osseointegration are generally preferred.[82,83]

Alopecia can be avoided with several technical adjustments.[7] First, it is stated that an incision with an angle of 30 degrees to the follicles preserves the deeper parts of these follicles and increases the number of hairs that grow back in the scar.[84] Second, tension on the sutures increases the width of the scar.[85] Also, minimal use of electrocoagulation may reduce hair loss, as well as lead to a reduced scar width.[7,78]

In the literature, calvarial bone graft harvesting has been associated with several perioperative and immediate postoperative complications related to dura exposure, including intraoperative dura fistulae. These complications were not reported in the included studies, and the incidence in previous reviews was low as well.[86–90] In fact, due to a recent adjustment of the technique, the incidence of such complications has decreased drastically.[5,86–91] However, to ensure safe harvesting, it is strongly advised that this is performed by a surgeon with experience in the technique and instrumentation.[5,86–91]

As reported in previous reviews,[2,67] the most important major complication following anterior iliac crest harvesting found in the current review was fracture of the crest resulting in the need to temporarily immobilize or walk with crutches. This usually heals uneventfully. A systematic review on morbidity following iliac crest harvesting advised careful patient selection, as osteopenia or osteoporosis, female sex, and advanced age may increase the incidence of iliac graft site fracture.[2]

A recent study comparing anterior iliac crest and calvarium bone grafts with respect to various indications, reported higher complication rates for both sites compared to the current review.[9] The discrepancy between these previous findings and those of the current review could be due to different indications and related patient factors, i.e. bone quality and healing capacity of the donor sites, and technical considerations, i.e. the harvesting techniques applied.

The conclusions drawn in this systematic review need to be interpreted with caution because of the large heterogeneity in study designs and the limited number of eligible studies. In general, most of the included studies had a high risk of bias and did not have a control group. Furthermore, the level of evidence of the meta-analysis is limited due to non-randomization in one of the studies. The studies demonstrated high patient satisfaction regardless of the donor site, although the reported outcomes for satisfaction included in the meta-analysis were ambiguous. To enhance the quality of the evidence in the future, it is suggested that RCTs comparing calvarial and anterior iliac crest harvesting should be

performed using pre-specified and well-defined protocols, with special emphasis on well-defined endpoints, i.e. PROs including sources of dissatisfaction to minimize reporting bias and an adequate sample size to minimize attrition bias. Also, well-defined standardized and validated measures to assess PROs, such as validated questionnaires and VAS scores for satisfaction and postoperative pain, should be used. Additionally, the reporting of patient characteristics including comorbidities and of the surgical technique, i.e. incision, graft harvesting, and donor site reconstructions, should be improved. Future studies should comply with the CONSORT guidelines to ensure high quality reporting of all aspects of the methodology and results.[92]

PROs as well as the complication rate could be affected by the type of surgical approach and the graft itself. Some of the included studies mentioned a variety of surgical approaches and methods of harvesting of the anterior iliac crest; for example, medial monocortical, lateral monocortical, bicortical, intracortical, and corticocancellous. The same is the case for the calvarium bone graft; for example, split in situ grafts, intracranial approach for splitting a parietal bone flap, different anatomical sites for harvesting the calvaria, and outer versus inner cortex grafts. Of the included studies, only a few described the surgical technique in detail. Where a description was provided, these studies used similar techniques. Therefore, a detailed analysis of the impact of different surgical techniques was not possible. Additionally it was decided not to report any information regarding the application of physiotherapy, as physiotherapy-related results were beyond the scope of this study. Furthermore, the included articles provided limited or no information on physiotherapy; moreover, the type and intensity of physiotherapy was consistently not provided. Therefore, the inclusion of this outcome in the present review paper would have possibly caused bias due to under-reporting in the included studies. It is strongly suggested that future studies consider the inclusion of the impact of surgical techniques or use of physiotherapy on PROs.

As the included studies recruited a wide range of populations, it was decided to investigate in general whether the patients perceived impairments in their daily living, and not go into specific detail. Furthermore, although the use of no foreign materials might be ideal from a biological point of view, it should be underlined that harvesting calvarial bone results in bone defects of square centimetres in magnitude and the harvested bone is of monocortical origin. In neurosurgery, however, (traumatic) skull defects are repaired using PMMA in the majority of cases, with favourable functional results.

Harvesting calvarial and/or anterior iliac crest bone grafts results in comparable patient satisfaction. Regardless of the donor site, the morbidity is low and generally temporary, and complications seldom occur. Subsequent adverse sequelae were not reported in the included patients. However, the findings on postoperative pain, disturbances in daily living, and complications are more in favour of calvarial harvesting when harvested with the adjusted technique. Thus, current available evidence shows that calvarial bone grafts are a viable alternative to anterior iliac crest bone grafts. Unfortunately, the risk of bias was high among the included studies. To enable a better understanding of the differences between the two harvesting sites, randomized controlled trials with validated and structured assessments of patient-reported outcomes are essential.

Ethical approval

Not applicable.

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Competing interests

None.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patient consent

Not applicable.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijom.2022.09.002.

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