Intraoperative culture positive allograft bone and subsequent postoperative infections: a retrospective review

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Background: Obtaining intraoperative cultures of allograft bone just before use in orthopedic procedures is standard practice in many centres; however, the association between positive cultures and subsequent surgical infections is unknown. Our study had 3 goals: to determine the prevalence of positive intraoperative allograft culture and subsequent infection; to determine if, in cases of subsequent infection, organisms isolated at reoperation were the same as those cultured from the allograft at the time of the index procedure; and to assess the costs associated with performing intraoperative allograft cultures.

Methods: In this retrospective case series, we obtained data on patients receiving allograft bone between 2009 and 2012. Patients receiving allograft with positive cultures were reviewed to identify cases of significant infection. Organisms isolated at reoperation were compared with the allograft culture taken at the time of implantation, and we performed a cost assessment.

Results: Of the 996 allograft bone grafts used, 43 (4.3%) had positive intraoperative cultures and significant postoperative infections developed in 2, requiring reoperation. Antibiotics based on culture results were prescribed in 24% of cases. Organisms cultured at the time of reoperation differed from those isolated initially. The cost of performing 996 allograft cultures was $169 320.

Conclusion: This series suggests that rates of positive intraoperative bone allograft culture are low, and subsequent infection is rare. In cases of postoperative infection, primary allograft culture and secondary tissue cultures isolated different organisms. Costs associated with performing cultures are high. Eliminating initial culture testing could save $42 500 per year in our health region.

Contexte : L'obtention de cultures d'allogreffes osseuses peropératoires juste avant une intervention orthopédique est une pratique standard dans de nombreux centres. Or, on ignore s'il y a un lien entre des résultats de cultures positifs et les infections chirurgicales subséquentes. Notre étude avait 3 objectifs : déterminer la prévalence des cultures d'allogreffes peropératoires positives et des infections subséquentes; déterminer si, dans les cas d'infections subséquentes, les agents pathogènes isolés lors d'une réintervention étaient les mêmes que dans les spécimens prélevés sur les allogreffes au moment des interventions initiales; évaluer les coûts associés à l'obtention des cultures d'allogreffes peropératoires.

Méthodes : Dans cette série de cas rétrospectifs, nous avons réuni des données sur des patients receveurs d'allogreffes osseuses entre 2009 et 2012. Nous avons passé en revue les cas d'allogreffes dont les résultats de culture étaient positifs pour recenser ceux qui étaient porteurs d'une infection significative. Nous avons comparé les agents pathogènes isolés lors de la réintervention à ceux de la culture de l'allogreffe effectuée lors de l'implantation, et nous avons procédé à une évaluation des coûts.

Résultats : Parmi les 996 allogreffes osseuses effectuées, 43 (4,3 %) avaient des résultats positifs aux cultures peropératoires; des infections postopératoires significatives se sont déclarées dans 2 de ces cas et ont nécessité une réintervention. Des antibiotiques ont été prescrits en fonction des résultats des cultures dans 24 % des cas. Les agents pathogènes isolés en culture au moment de la réintervention étaient différents de ceux qui avaient été initialement isolés. Le coût des 996 cultures d'allogreffes s'est élevé à 169 320 $.

Conclusion : Cette série donne à penser que les taux de résultats de cultures d'allogreffes osseuses peropératoires positifs sont bas et que les infections subséquentes sont rares. Dans les cas d'infections postopératoires, les cultures des allogreffes primaires et les cultures tissulaires secondaires ont révélé la présence d'organismes pathogènes différents. Les coûts associés à la réalisation des cultures sont élevés. Éliminer les cultures initiales permettrait à notre région de santé d'économiser 42 500 $ par année.

The use of allograft bone has become increasingly common in orthopedic surgery,[1,2] specifically in spinal fusion, revision arthroplasty and tumour reconstruction.[3] Policies differ from country to country[1,4–11] with respect to how allograft bone is processed and tested from the time of harvest to the time of implantation. In some centres the standard is to obtain a sample of the allograft bone intraoperatively for culture just before implantation as a quality control measure. The average positive intraoperative allograft bone culture rate reported in the literature ranges from 1.4% to 12%.[4,7,9,11–13] Although some studies comment that cases of positive culture taken at the time of implantation went on to develop wound infections,[2,6] most studies suggest that these positive cultures do not correlate with postoperative infections and that the organisms isolated in the postoperative infection are only rarely the same as those isolated in the intraoperative allograft culture.[9,10,12,14,15] It is difficult to apply these results to all populations, as national policies for handling allograft bone differ.

Furthermore, there is no clear evidence to guide surgeons in dealing with positive results. Importantly, a positive culture from the graft obtained at the time of implantation often represents a contaminant and does not necessarily represent a graft infection. Some centres have instituted a protocol that treats all patients with a positive intraoperative culture with empiric antibiotics.[7] One study found no significant postoperative infections related to positive intraoperative bone allograft cultures when patients with positive cultures were treated with 500 mg of Cefadroxile twice daily for 3 weeks; however, the authors stated there was little evidence for this protocol, and it was not compared with other regimens.[7] Most centres do not have a treatment protocol for patients with positive allograft cultures, and practices range from providing no empiric antibiotic treatment in patients with positive intraoperative allograft cultures to providing empiric intravenous antibiotic therapy.[7,14]

There is a paucity of evidence supporting the practice of obtaining intraoperative allograft culture before implantation and little consensus on how to treat patients with positive results. Few studies have examined whether organisms cultured from the initial allograft at transplantation correlate with those isolated in cases of subsequent postoperative infection. The impact of positive intraoperative allograft cultures is largely unknown and may not alter management. Results of intraoperative allograft cultures typically take days to be reported, often after the patient has been discharged home. In our centre, quality control is guided by The National Standard of Canada CAN/CSA: Tissues for Transplantation guidelines.[16–18] The rate of positive intraoperative allograft bone culture has not been reported at our centre. Further, there is an added cost to the health care system to perform intraoperative allograft cultures. To our knowledge no cost assessment has been performed. If there is no association between positive intraoperative allograft culture and postoperative infection, potential health care dollars may be saved.

We sought to answer the following through this study: What is the prevalence of positive intraoperative allograft bone culture and subsequent postoperative infection at our centre? In cases of subsequent postoperative infection, are organisms isolated at reoperation the same as those cultured from the original allograft? What are the costs associated with performing intraoperative allograft cultures compared with the costs of treating subsequent postoperative infections?

Methods

Study design

Following approval from the ethics board, we carried out a retrospective review of patients receiving allograft bone at our centre between Jan. 1, 2009, and Dec. 31, 2012. Our regional transplant program database was used to identify all patients receiving allograft bone (structural or cancellous) in our health region during the study period. This yielded a sample size of 996 patients. Patients with positive intraoperative allograft bone cultures at the time of transplantation were identified and included for further analysis. These charts were obtained from health records and reviewed retrospectively for the first postoperative year. Patients with negative intraoperative allograft cultures were not reviewed. Patients with pre-existing infection before receiving allograft bone were excluded. No other exclusion criteria were used.

Patients with significant postoperative infection in the first postoperative year were identified. Significant infection was defined as requiring reoperation for infection or requiring a course of intravenous antibiotics for infection related to the original surgery. Patients with superficial wound erythema who did not require reoperation and patients receiving an outpatient course of oral antibiotics were not considered to have a significant postoperative infection, as these are unreliable indicators of infection and do not represent costly interventions or substantial patient harm. Treatment practices for positive intraoperative allograft cultures with antibiotics were recorded, as this is not standard at our centre and could influence the development of a postoperative infection. No differentiation between deep surgical site infection and graft infection were made, as these typically occur together.

We calculated the overall rate of intraoperative culture-positive allograft bone at the time of transplantation at our centre and compared it with reports from other centres. In cases of postoperative infection where new cultures were taken at the time of reoperation, we compared the results with the organisms found in the allograft culture obtained at the time of implantation. Finally, we assessed the costs

associated with performing intraoperative allograft bone cultures, prescribing empiric antibiotic treatment for positive results and the treatment of postoperative infection.

Bone bank protocol

In our centre, the majority of bone allograft comes from the femoral heads of living donors receiving total hip arthroplasty and from deceased bone donors. The National Standard of Canada CAN/CSA: Tissues for Transplantation guides the retrieval process, processing and implantation process at our centre.[16–18] Donors are screened for transmissible diseases, including hepatitis B and C, HIV and syphilis. Bone is retrieved in a sterile fashion and wrapped in sterile drapes. Two morsels of bone tissue from 2 separate locations of each graft are cultured at the time of retrieval by the operating room staff using new sterile instruments. Samples are not swabbed for culture, as this has been shown to be an ineffective means of identifying contamination.[19] If these initial cultures are positive, the bone is discarded and is not used for transplantation. No further processing, antibiotic treatment, or irradiation takes place after retrieval. Bone is then stored in sterile containers at –80°C and is kept for up to 5 years. If the bone is reprocessed for any reason, new cultures are taken, as this represents a potential source of contamination. Reprocessing is exceedingly uncommon at our centre, therefore this is rarely performed. The National Standard of Canada CAN/CSA: Tissues for Transplantation states that bone banks must either have a bioburden reduction protocol or obtain allograft samples for culture at the time of transplantation. As our centre does not have a bioburden reduction protocol, new allograft cultures are taken intraoperatively at the time of transplantation, just before its use. This is performed by the operating room staff in a sterile fashion with separate instruments before the graft comes into contact with the recipient. At all stages, cultures are performed for both aerobic and anaerobic organisms and for both rapid and slow-growing organisms. Allograft is thawed in the operating room at room temperature or in warmed sterile saline. No irrigation or antibiotic is added at this time. The result of this second culture taken just before transplantation is the point of interest for the present study.

Results

Between January 2009 and December 2012, 996 allograft bone grafts were used in our health region. Of these, 43 (4.3%) had a positive intraoperative culture and were included for analysis. Six patients were excluded based on predefined criteria — 5 because bone graft was used in the setting of a previous infection and 1 because both bone and tendon grafts were used with only the tendon graft having positive intraoperative cultures. This left 37 patients with allograft bone grafts for final analysis; 46% were men (Table 1). All patients received standard prophylactic antibiotics at the time of their index procedure. Empiric antibiotics based on a positive intraoperative allograft culture result were prescribed in 9 (24%) patients. Practices were heterogeneous among surgeons, with no treatment choice used more than once. From all allograft samples included in this analysis, 13 different organisms were isolated from intraoperative cultures. Table 2 illustrates cultured organisms and their respective incidences. *Staphylococcus epidermidis* was most commonly isolated (22%). In total 46% of positive cultures occurred in spine cases; 29% in revision arthroplasty cases; and 24% in other cases, such as trauma.

Two of the 37 (5.4%) patients in our study experienced a significant postoperative infection, both requiring reoperation. In each case, cultured organisms isolated at the time of reoperation and blood cultures differed from the original allograft culture. In the 2 cases of significant postoperative infection, the first patient received allograft bone for a lumbar spine fusion, which grew *Corynebacterium diphtheriae* at initial intraoperative culture. Cultures taken at the time of irrigation and débridement were positive for *S. epidermidis* and *Staphylococcus warneri*. The second patient received allograft bone for a posterior spinal fusion, which grew *Bacillus* at initial intraoperative culture. Subsequent cultures taken at the time of irrigation and débridement were positive for *S. epidermidis*. Neither patient received specific empiric antibiotic therapy; however, the second patient was on intravenous antibiotics (piperacillin/tazobactam, which has broad coverage) during the entire postoperative period for a separate infection (pneumonia) that developed postoperatively. Aside from these 2 patients, an additional 4 patients with positive intraoperative allograft cultures underwent reoperation for other reasons (revision procedures, hardware removal). None of these patients demonstrated clinical signs of infection at the time of reoperation.

The cost of performing an intraoperative culture at our centre is $170. The cost of performing 996 allograft bone cultures was therefore $169 320. Antibiotic choice affects the costs associated with empiric use in cases of positive intraoperative allograft cultures. Table 3 illustrates the cost per day associated with commonly prescribed antibiotics. In this series, treatment of positive allograft cultures varied from no antibiotics to short courses of oral antibiotics to longer courses of intravenous antibiotics (Table 1). The total cost for empiric antibiotics used in this study period was approximately $3500. Irrigation and débridement costs anywhere from $1755 to $2646, depending on the area of the body. This includes the cost of the surgeon, nurses and anesthesiologist. Patients requiring irrigation and débridement typically receive a course of 6 weeks of intravenous antibiotics following surgery, which costs anywhere from $1602 to $3716, depending on the choice of antibiotic. On average, our centre uses 250 bone allografts per year. The

annual cost of performing allograft cultures is therefore $42 500. The annual cost to our health care system associated with these cultures is greater when the use of empiric antibiotics is taken into account.

Discussion

This series demonstrates that the incidence of positive intraoperative allograft bone cultures is low and that subsequent postoperative infections are rare. Further, when postoperative infections occur, organisms isolated at reoperation differ from those isolated in the initial allograft culture. In a recent project, NOTIFY, bacterial transmission caused by a bone allograft was defined as having the same organism cultured from both the graft and the recipient.[2] The rate of positive intraoperative bone allograft culture in our series was 4.3%, consistent with rates reported in other centres.[7,9,10,12,15] Furthermore, subsequent postoperative infection following a positive intraoperative positive allograft culture was rare, occurring in 2 of

Table 1. Patient characteristics

Patient	Procedure type	Allograft culture result	Empiric antibiotics prescribed	Postoperative infection
1	Arthroplasty	*Staphylococcus warneri* CONS	None	None
2	Foot and ankle	*Staphylococcus capitis*	None	None
3	Arthroplasty	*Streptococcus viriden*	None	None
4	Trauma	CONS	None	None
5	Arthroplasty	*Staphylococcus warneri*	None	None
7	Arthroplasty	*Corynebacterium* Anaerobes	None	None
9	Arthroplasty	CONS	Cefazolin 3 d	None
10	Arthroplasty	*Conynebacterium*	None	None
11	Spine	*Bacillus*	None	*Staphylococcus epidermidis*
13	Trauma	*Bacillus*	Cefazolin 3 d Cephalexin	None
14	Spine	*Staphylococcus capitis*	None	None
15	Trauma	*Corynebacterium* *Staphylococcus aureus*	None	None
16	Spine	CONS	None	None
17	Trauma	*Staphylococcus epidermidis* Gram-positive bacilli	None	None
18	Arthroplasty	CONS	None	None
19	Spine	*Bacillus*	Cefazolin 8 d	None
20	Spine	*Staphylococcus hominis*	Cefazolin 3 d, then cephalexin 2 mo	None
23	Arthroplasty	*Staphylococcus epidermidis*	None	None
24	Foot and ankle	CONS	None	None
26	Spine	*Staphylococcus epidermidis*	Ceftriaxone 4 wk	None
27	Spine	*Staphylococcus epidermidis*	Vancomycin	None
28	Arthroplasty	*Bacillus*	None	None
29	Spine	CONS	None	None
30	Spine	*Corynebacterium diphtheriae*	None	*Staphylococcus epidermidis* *Staphylococcus warneri*
31	Spine	*Bacillus*	None	None
32	Spine	*Staphylococcus capitis*	Cephalexin 7 d	None
33	Spine	*Yarrowia lipolytica*	None	None
34	Arthroplasty	*Staphylococcus epidermidis*	None	None
35	Arthroplasty	*Staphylococcus epidermidis*	None	None
36	Spine	*Veillonella parvula*	Metronidazole 6 wk	None
37	Spine	*Corynebacterium*	None	None
38	Sports	*Lactococcus garvieae*	None	None
39	Spine	CONS	None	None
40	Spine	*Staphylococcus epidermidis*	None	None
41	Trauma	*Bacillus*	None	None
42	Spine	*Staphylococcus warneri*	None	None
43	Trauma	*Staphylococcus epidermidis*	None	None

CONS = coagulase-negative *Staphylococcus aureus*.

37 (5%) patients in our series. Importantly, during our 4-year study period, no postoperative infection could be linked to a positive allograft bone culture. Practices for dealing with positive cultures in our centre are inconsistent and are not based on conclusive evidence. Performing initial intraoperative cultures is costly, and in the majority of cases positive findings did not change clinical management, with 73% of patients receiving no empiric antibiotic. The cost of prophylaxis varies with antibiotic choice and health region, ranging from $1.92 per day to $88.49 per day. Postoperative infection does not appear to be linked to initial intraoperative allograft bone culture, and thus performing these cultures is unlikely to prevent cases of postoperative infection. Considering that organisms differed in cases of postoperative infection, outcomes of our cost assessment are not in favour of performing intraoperative allograft cultures. To our knowledge, no previous study has examined the costs associated with performing intraoperative allograft cultures. In Canada, several centres no longer perform intraoperative allograft cultures on a routine basis, although cultures may be requested by the treating physician. Instead, a bioburden reduction protocol must be in place.[16,18] It is unclear if this has resulted in cost savings. Our study suggests that even in the absence of a bioburden reduction protocol intraoperative allograft cultures are not clearly linked with postoperative infections and remain an added cost to our system with unclear benefit.

Use of allograft bone in recent years continues to increase.[1] Although the use of autograft bone remains the gold standard,[20] allograft bone is advantageous for several reasons, including unlimited and rapid supply as well as decreased donor site morbidity.[7,20] Several studies have examined complications of allograft bone, including infection, both for the donor[13,21–23] and recipient.[1,2,4,6,7,9,12,15,20,24,25] Several studies examining the link between allograft bone and postoperative infection have cited various results, some attributing postoperative infection to allograft bone[2,6] and others to infection rates inherent with these often more complex procedures.[2,7,9,10,20] Postoperative infections in these cases are devastating complications and can be difficult to manage. Avoidance of infection is of the utmost importance.

Table 2. Intraoperative allograft bone cultures

Organism	Incidence, %
Staphylococcus epidermidis	21
Coagulase-negative *Staphylococcus* species	21
Staphylococcus warneri	8
Staphylococcus capitus	8
Corynebacterium	11
Bacillus	16
Other	16

Table 3. Daily antibiotic costs (Canadian)

Medication	Cost/d, $
Cephalexin	1.92
Cefazolin	38.16
Ceftriaxone	37.50
Piperacillin/tazobactam	64.44
Clindamycin	2.66
Trimethoprim/sulfamethoxazole	0.24
Vancomycin	88.49

Similar studies have focused on allograft bone used specifically in spine procedures.[7,20,26] In a retrospective review by Barriga and colleagues,[7] 22 of 189 bone allografts had positive intraoperative cultures, none of which went on to develop significant postoperative infections. Patients with positive intraoperative allograft cultures in that series were treated prophylactically with cefadroxile for 3 weeks, regardless of the organism cultured.[7] The authors stated that this prophylactic regimen was not based on evidence, and they concluded that positive intraoperative allograft bone cultures were likely due to contamination either in the operating room or at the time of harvest, initially undetected.[7] They recommend continuing the practice of obtaining intraoperative allograft bone cultures to identify patients suitable for antibiotics, but suggest that no other treatment is required to prevent infection.[7]

In the retrospective study by Couture and Cabana[20] of patients receiving bone graft for spine procedures, rates of infection between autograft and irradiated allograft bone were compared. They found no statistical difference in rates of positive intraoperative culture. They concluded that there was no evidence to suggest that a positive intraoperative allograft culture reliably predicts postoperative infection and called into question the cost benefit of this procedure.[20] They did not correlate organisms cultured at reoperation with those obtained at the initial allograft culture and suggested that further research examining the utility of intraoperative allograft bone culture with larger sample sizes and adequate control groups is warranted.[20]

There is limited literature assessing the utility of intraoperative bone allograft culture and treatment of a positive culture result. Previous studies are small, single-centre reviews, most of which concluded that cases of postoperative infection could not be clearly linked with positive intraoperative allograft bone cultures at initial surgery.[7,9,10,15,20,27] In a retrospective study by Van de Pol and colleagues,[9] 48 of 426 patients receiving allograft bone were found to have positive intraoperative cultures. Three of these patients went on to experience significant postoperative infections; however, only 1 patient was found to have the same organism isolated from the original allograft culture.[9] The authors concluded that positive intraoperative allograft cultures represented contamination that was unlikely to cause subsequent postoperative infection and that intraoperative bone allograft cultures were unnecessary.[9]

Our results mirror these findings, with only 2 patients experiencing significant postoperative infections following positive allograft bone culture. Further supporting the conclusions of Van de Pol and colleagues,[9] many of the organisms isolated from allograft cultures are known skin contaminants.

Limitations

This study has a number of limitations. First, the cases of patients with negative allograft cultures were not reviewed, and thus no statistical analysis was possible owing to a lack of a control group. Our aim in this series was to associate organisms found in postoperative infections to those of the intraoperative allograft culture taken at the time of implantation, not to compare infection rates in those with positive allograft cultures compared with those with negative cultures. Second, we could not control for heterogeneous practices in dealing with positive allograft cultures owing to the retrospective nature of this study. Although this practice may be costly, it did not result in differences in outcomes for patients in this series. Finally, postoperative infection following positive allograft cultures was a rare occurrence, observed in only 2 patients in this series. It may be difficult to draw conclusions from this small number; however, the fact that this occurrence was small shows that postoperative infections following positive allograft cultures are rare.

Conclusion

We found rates of positive intraoperative allograft bone cultures in our centre to be low and subsequent postoperative infections rare, calling the utility of intraoperative allograft cultures into question. In the vast majority of cases with positive allograft cultures, management was not changed. Patients receiving unnecessary antibiotics for positive allograft cultures represent an area of potential patient harm and unnecessary health care spending. In our entire study period, no case of postoperative infection could be clearly linked to a positive allograft culture. Obtaining these cultures is costly; we estimated yearly savings of $42 500 in our health region alone if cultures were eliminated. Other centres that have eliminated intraoperative allograft cultures instead perform alternative protocols for allograft treatment. Our series suggests that even in the absence of these various protocols, allograft cultures do not predict cases of postoperative infection. Further investigation of potential savings on a national level, taking into account various methods of allograft handling, would provide valuable additional information. Continued research in the form of a prospective multicentre trial would help to clarify which measures, if any, reduce postoperative infections as well as the potential impact of these cost savings.

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