COST-UTILITY OF VARIOUS BIOLOGIC VERSUS ENDOPROSTHETIC RECONSTRUCTION FOR PRIMARY BONE SARCOMA OF THE HUMERUS

Sittichoke Watcharamasbonkkot, Thipachart Punyaratabandhu, Phutsapong Srisawat, Puwadon Veerapan

Department of Orthopedics, Phramongkutklao Hospital, Bangkok, Thailand.

Abstract

Background: The development of bone sarcoma treatment has resulted in a higher survival rate of patients including the developed surgical treatment called limb salvage surgery. Reconstructive surgery plays a vital role among patients and their quality of life after treatment. However, cost-effectiveness is another crucial factor in choosing a treatment method.

Methods: Eighteen patients with osteosarcoma were recruited in this study. All were treated using limb salvage surgery. The data were collected using the utility coefficient from the EQ-5D-5L Health Questionnaire. The patient's medical cost was obtained from Phramongkutklao Hospital, and all data were calculated for cost-effectiveness using the cost-utility analysis.

Results: Endoprosthesis reconstruction exhibited the highest utility value of 0.85 QALY and the lowest treatment complications. Nevertheless, the most increased cost was an average of 238,432.34 THB. In terms of cost, the recycled autograft showed the lowest treatment cost at an average of 60,774.61 THB. However, the complication of this method was quite severe, with a 50% recurrence rate. Allograft reconstruction was the most cost-effective method with a lower cost than endoprosthesis reconstruction (61,341.40 THB), despite having a lower utility of 0.49 QALY.

Conclusion: This study reported that endoprosthesis reconstruction resulted in more optimistic patient well-being but still indicated high cost. Using one-way sensitivity analysis, the QALY gain was only 16.9% of Thai per capita. When the cost of endoprosthesis reconstruction was reduced by only 15%, it could replace allograft reconstruction. In addition, an increase of the QALY, gaining only 20% of the average Thai per capita, would be cost-effective when the expense of endoprosthesis reconstruction was reduced by 4%.

Keywords: Primary bone sarcoma, Humerus bone cancer, Bone reconstruction, Cost-utility analysis, Various biologic reconstruction, Endoprosthesis reconstruction

J Southeast Asian Med Res 2023: 7: e0152
https://doi.org/10.55374/jseamed.v7.152

Correspondence to:
Watcharamasbonkkot S, Department of Orthopedics, Phramongkutklao Hospital, 315 Rajvithi Road, Bangkok 10400, Thailand
Email: birdsw@hotmail.com

Received: 26 December 2022
Revised: 31 May 2023
Accepted: 5 June 2023

Introduction

Bone sarcoma, a tumor that forms in bone tissue, is most often diagnosed among people under age 35.[1] Tumors are found on the limbs more than in other regions.[1] This defect affected the patient's quality of life. The development of cancer treatment has improved the survival rate of patients[2]; moreover, limb-salvage surgery was developed helping to preserve the patient's limbs.[3, 4] This study discussed bone replacement surgery after tumor removal. The study aimed to compare the cost-effectiveness in terms of cost-utility, namely, the health economy process, to use as treatment decision-making information to enhance the best benefit for the patient's future quality of life of bone cancer.

From the relevant literature review search involving PubMed and Google Scholar, using the keywords "Musculoskeletal sarcoma and functional outcome and Evaluation and Health-related quality of life and cost-effectiveness and cost-utility," no study was found concerning assessing cost-utility analysis regarding bone cancer treatment in Thailand. However, only one study by Wilson et al. described the comparison of reconstruction surgery in primary bone sarcoma of the knee.[4] Additionally, Sande et al. only focused on the results of various surgery techniques without comparing their effectiveness. [5] It reported the metallic replacement method for patients with bone sarcoma, receiving reconstruction of the proximal humerus after cancer excision, showing a lower side-effect rate than using bone from donors. Moreover, the metallic replacement method established a significantly higher implant survival rate and better functional results than using donated bone. Nonetheless, patients still needed help with the metallic replacement method because the cost was high. The study aimed to assess the cost-utility of reconstructive surgical procedures with various biological reconstruction techniques, i.e., osteoarticular allograft and recycled bone autograft, compared with endoprosthetic reconstruction among patients with primary bone sarcoma of the humerus.

Methods

This research constituted a retrospective analysis study targeting patients with primary bone sarcoma of the humerus undergoing limb-sparing surgery at the Department of Orthopedics, Phramongkutklao Hospital, from 2012 to 2022. The study was approved by the Institutional Review Board of the Royal Thai Army Medical Department, IRBRTA 1386/2565. The study included all patients receiving a diagnosis of primary bone sarcoma of the humerus and those undergoing limb-sparing surgery. Patients having a distant metastasis or recurrent lesion area were excluded when assessed using the EQ-5D-5L Health Questionnaire. Those who could not be assessed using the EQ-5D-5L Health Questionnaire or did not voluntarily provide additional information in the case of incomplete information in the PMK Musculoskeletal Oncology Patient Database (PMK-MOPD) were also excluded. In total, 18 patients met the requirements.

Permission to access expenses information was requested including medical costs from medical records, hospital patient billing data and funds that the National Health Security Office (NHSO) reimbursed to the hospital according to the Joint Disease Diagnosis Group (DRG) charges from the director of Phramongkutklao Hospital.

EQ-5D-5L Health Questionnaires were used to collect assessment information from the database PMK-MOPD. When any incomplete form was found, the researcher contacted the patient for more details with an understanding of informed consent.

Cost-utility of medical treatment was calculated using the currency in THB per quality adjusted life-year (QALY) accessed by life year-gained (LYG) with utility from EQ-5D-5L Health Questionnaire assessment and literature review.

Outcome Measurement

The QALY was obtained using the utility coefficient from the EQ-5D-5L Health Questionnaire. The QALY revealed the database displaying the health status of each surgery method in Thailand, leading to cost-utility analysis comparing the cost-effectiveness of different surgical procedures with direct medical costs.

Data Collection

Demographic data: The demographic data were collected from the patient's database at the Musculoskeletal Oncology Unit, Department of Orthopedics, Phramongkutklao Hospital; PMK Musculoskeletal Oncology Patient Data (PMK-MOPD), consisting of the physical and clinical data of participants.

Cost: In this study, we focused only on direct medical costs, comprising the patient hospital charges and the National Health Security Office (NHSO) reimbursements to the hospital according to the Diagnosis-Related Group (DRG charge). The reasons for using those costs were that they represented the same standard in all areas without confounding factors (such as economic status, travel expense and living expense), and could be measured. All patients assumed direct nonhealth care and indirect costs equally. The direct nonhealth care costs consisted of travel, accommodation, meals and the time value of informal care lost. The indirect costs comprised the cost of sick leave because the patient might have been unable to remain active and maintain a daily life on a sick day.

Utilities: The utility data were obtained from the patient's database at the Musculoskeletal Oncology Unit, Department of Orthopedics, Phramongkutklao Hospital; PMK Musculoskeletal Oncology Patient Data (PMK-MOPD) and were collected using the EQ-5D-5L Health Questionnaire assessment format. Grobet et al. showed that the utility value of the metallic replacement method was 0.85 and reduced by 25% per the QALY when the revision surgery was performed. [6] Losina et al.[7] and Gundle et al.[8] demonstrated that the utility value among patients requiring limb amputation after conservative treatment was 0.48 per the QALY (0.48). Wilson et al. revealed that the utility values among patients with non-operative complications such as infection were reduced by 12.5%. [9]

Data analysis

Health value or the QALY, which was obtained from the EQ-5D-5L questionnaire, was acquired in the utility value when multiplied by the number of LYG, in which the general cancer treatment standard was used, and the cancer was considered cured after ten years of follow-up without noting a recurrence of the disease. Here, the indication of cost-effectiveness in a QALY was represented by a COST/QALY value, also known as the cost-utility, which was obtained by quantifying the cost of each treatment option per QALY. Moreover, this study also revealed the surgery method showing the most cost-effectiveness when comparing the QALY gain ratio, i.e., the ratio between the cost and healthy years of the two surgeries compared.

Finally, the cost-effectiveness could be forecasted when the cost of each method was reduced to an acceptable value. This result was called one-way sensitivity analysis, which showed a cost-effectiveness acceptability curve. The curve represented the relationship between the willingness to pay per QALY (x-axis) and the probability that the choice would be worthwhile (y-axis).

Results

The patient database showed 32 patients meeting the study inclusion criteria. The patients were divided in two groups: 30 receiving bone tumor resection and reconstruction and two needing amputation because cancer had spread too much in nearby areas. However, 12 of all patients were excluded due to: 1) the spread of a tumor or cancer to distant parts of the body from its original site (n=8), 2) the postoperative recurrence of the tumor at the original site before completing the EQ-5D-5L questionnaire (n=1) and 3) the incomplete response of the EQ-5D-5L questionnaire (n=3).

The mean age of the included patients was 24.56 years, ranging from 9 to 45 years. Since patients received their first treatment, the follow-up time was 331 to 1,567 days (an average of 889 days). The male ratio was relatively higher than that of females (male-to-female ratio = 10:8). Only the two most common types of diagnosed cancers were included, namely, osteosarcoma (n=12) and Ewing sarcoma (n=6), occurring more often right- than left-sided **(Table 1).**

Table 1. Patient characteristics

Data	Content	Number (Total 18)	%
Gender	Male	10	55.56
	Female	8	44.44
Diagnosis	Osteosarcoma	12	66.67
	Ewing sarcoma	6	33.33
Side	Right	10	55.56
	Left	8	44.44

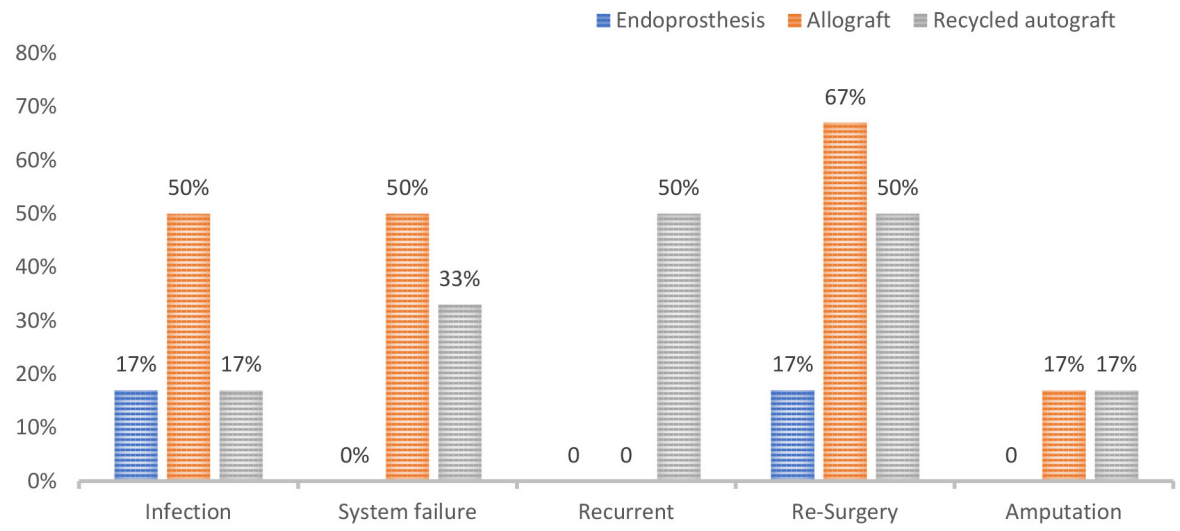

Figure 1. Complications of reconstruction methods

Regarding the incidence of complications, patients with metallic endoprosthetic reconstruction had the lowest rate of developed complications, comprising only one case. However, the revision surgery was completed, while other reconstructive surgery methods presented more complications. Six patients showed complications with allograft reconstruction, divided into three patients with infection and three patients with systemic failure, of whom four patients underwent revision surgery, and one had an arm amputated because of uncontrollable complications. Three patients presented complications in recycled autograft surgery, divided in one patient with infection and two patients with systemic failure. However, this was the only treatment that presented three cases of recurrence. All patients had undergone revision surgery. Those complications directly affected the utility value among three patients, one needing amputation, as shown in **Figure 1.**

This study obtained the utility value from the patient's database at the Musculoskeletal Oncology Unit, Department of Orthopedics, Phramongkutklao Hospital; PMK Musculoskeletal Oncology Patient Data (PMK-MOPD). The EQ-5D-5L Health Questionnaire assessment format was used to determine the utility value (Utility, U) according to the Health Technology Assessment Handbook for Thailand. (10) The literature review indicated that the utility value of metallic endoprosthesis reconstruction was the highest [6] compared with allograft and recycled autograft reconstruction (0.85QALY, 0.49QALY and 0.41QALY, consecutively) **(Table 2)**

This current study found that the average cost of endoprosthesis reconstruction was higher than other biologic reconstructions, having equivalent values (238,432.34 THB and 61,502.57 THB, respectively). The comparison of QALY showed that the allograft reconstruction was the most promising cost-effective method; however, focusing

Table 2. Utility of patients, based on reconstruction methods and complications.

Parameter	Utility	References
Reconstruction Methods		
Endoprosthetic Reconstruction	0.85 QALY	Grobet CE et al.[7]
Osteoarticular Allograft	0.49 QALY	PMK-MOPD
Recycled Bone Autograft	0.41 QALY	PMK-MOPD
Biologic Reconstruction (Allograft & Recycled Bone Autograft)	0.44 QALY	PMK-MOPD
Each Re-Surgery	↓25%	Losina E et al.[8]
Amputation	0.4800 QALY	Gundle KR et al.[9]
Non-Operative complications	↓12.5%	Wilson RJ et al.[5]

Table 3. Cost-utility analysis of reconstruction methods compared with endoprosthesis

Reconstruction Methods	Cost	QALY	Cost/QALY	QALY gain (Compare with Endoprosthesis)
Endoprosthesis	238,432.34 (180,653.76 – 300,323.55)	8.5	28,050.86	
Allograft	61,341.40 (31,152.98 – 109,132.44)	4.9	12,518.65	49,191.93
Recycled Bone Autograft	60,774.61 (21,017.71 – 98,115.03)	4.1	14,823.08	40,376.76
Biologic (Allograft & Autograft)	61,502.57 (21,017.71 – 109,132.44)	4.4	13,977.86	43,153.60

on only the health outcome displayed that the high utility treatment constituted a healthy person treated with endoprosthesis reconstruction. Therefore, further comparing the cost-effectiveness of different reconstructive surgery methods was needed individually. Those results are exhibited as the QALY gain in **Table 3.** Data were also analyzed using a one-way sensitivity method, as shown in **Table 4.**

Discussion

This study analyzed the data of patients treated in Thailand's healthcare context. The study showed no difference between the service and medical expenses. This differs from foreign countries because services were provided mainly by nonprofit agencies in Thailand, such as the cost of bone donor services and disinfection and storage, not including inpatient expenses. This study represented medical service data relevant to real-life situations in Thailand.

This data set concluded no difference in the patient's demographic data including age, sex, diagnosis and skills and the choice of reconstruction method after tumor resection. Then it could imply an important cost factor suitable for each patient, affecting different treatment outcomes. This study emphasized the QALY, which was obtained from various factors such as the use of postoperative

Table 4. Sensitivity analyses of price-discounted endoprosthetic reconstruction

Situation	Cost (Baht)	QALY gain
Price Discounted for Balance Utility		
Substitute Osteoarticular Allograft	106,408.55 (↓55.37%)	12,518.65 (5.40%N*)
Substitute Recycled Bone Autograft	125,408.55 (↓47.16%)	14,823.08 (6.40%N*)
Substitute Various Biologic Reconstruction	118,811.81 (↓50.17%)	13,977.86 (6.00%N*)
Price Discounted by 15%		
Substitute Osteoarticular Allograft	202,667.49 (↓15.00%)	39,257.25 (16.90%N*)
Substitute Recycled Bone Autograft	202,667.49 (↓15.00%)	32,248.38 (13.90%N*)
Substitute Various Biologic Reconstruction	202,667.49 (↓15.00%)	34,430.47 (14.80%N*)
Price Discounted for use 20% of N*		
Substitute Osteoarticular Allograft	228,496.67 (↓4.00%)	46,432.02 (20.00%N*)
Substitute Recycled Bone Autograft	265,075.50 (↓----%)	46,432.02 (20.00%N*)
Substitute Various Biologic Reconstruction	251,873.85(↓----%)	46,432.02 (20.00%N*)

N: NESDC Economic Report 15th August 2022; Office of the Economic and Social Development Council, Thailand

organs, pain, anxiety and overall satisfaction. All collected data were displayed as the utility value. Moreover, these data also indicated the treatment complications. The allograft reconstruction had the most complications of infection and system failure, resulting in patients undergoing repeated surgery, including amputation. The recycled autograft surgery had complications of undergoing revision surgery. All these complications were included in the utility analysis. The data suggested that the surgery with the endoprosthetic reconstruction method exhibited the highest utility value, meaning the patient was most satisfied with the treatment involving endoprosthetic reconstruction. In addition, a low complication rate was observed using this surgical method. The surgical expense of allograft reconstruction was lower than that of endoprosthetic reconstruction; therefore, the cost-effectiveness assessment in cost-utility showed that allograft reconstruction was the most cost-effective, followed by recycled autograft. Even though allograft reconstruction indicated the lowest cost, recurrent disease occurred. Because the recurrent illness was a significant complication affecting well-being postoperation among patients, this surgical method was not cost-effective in terms of QALY.

This study also investigated the development opportunity for surgery-based methods because the endoprosthesis reconstruction presented the highest utility value and the fewest complications from treatment. Therefore, the QALY gain of this method was calculated. Comparing the other surgical methods that were more cost-effective, developing surgical methods by endoprosthesis reconstruction was as cost-effective as the allograft reconstruction method, which was the most cost-effective, with the additional investment required per QALY in the amount of 49,191.93 THB, the same as the other biologic reconstruction treatments. In **Table 4**, when the cost of endoprosthesis reconstruction decreased by 55.37% at 106,408.55 THB, allograft reconstruction would be as cost-effective as the most cost-effective surgical method. However, reducing those costs by 15% at 202,667.49 THB required the additional investment for a QALY gain of only 39,257.25 THB or only 16.9% of the average Thai per capita in 2021, according to the announcement in the 2022 economic projections of the Office of the National Economic and Social Development Council August 15, 2022 (NESDC Economic Report 15th August 2022; Office of the Economic and Social Development Council, Thailand).[11] Reducing costs by only 15%

would make the most cost-effective treatment method compared with the cheapest technique, recycled autograft. Therefore, additional investment for a QALY of only 13.9% of the average Thai per capita would be required. When starting with Thai per capita, if we invest more for an additional QALY gain at 2% of the average income of Thai per capita or 46,432.02 THB, the endoprosthesis reconstruction cost was required to drop by 4% or 228,496.67 THB. This data suggested that we could use this surgical method instead of the most cost-effective technique, allograft reconstruction. This additional investment benefits a patient who has undergone surgery to be healthy after surgery, without risk of complications from allograft reconstruction surgery. It could also reduce the cost of treating complications.

Conclusion

Endoprosthesis reconstruction presented the highest utility value with high patient satisfaction and minimal complications. Employing this method at the total price could replace the most cost-effective technique, allograft reconstruction, but required an additional investment for the QALY gain of 39,257.25 THB, or only 16.9% of the average income of Thai per capita. Reducing the surgery price by only 15% when the investment was only 32,248.38 THB, or only 13.9% of the average Thai per capita would permit using this method instead of the cheapest operation, recycled autograft. In addition, when we invest 20% of the average income of Thai per capita or 46,432.02 THB, the endoprosthesis reconstruction cost will drop by 4%. This surgical method would be comparable with the most cost-effective technique, allograft reconstruction.

References

1. Darling J. A different view of sarcoma statistics. ESUN 2007; 4: 1-7. http://sarcomahelp.org/articles/sarcoma-statistics.html
2. DeVita VT, Lawrence TS, Rosenberg SA. Principles and Practice of Oncology. Lippincott Williams & Wilkins 2019; 11: 2037-68.
3. Julian MS, Garcia BV. Biological reconstruction in bone sarcomas: Lessons from three decades of experience. Orthop Surg 2016; 8: 111-21.
4. American Joint Committee on Cancer. Bone. In: AJCC Cancer Staging Manual. 8th ed. New York, NY: Springer; 2017: 471-86.
5. Wilson RJ, Sulieman LM, VanHouten JP. Halpern J, Schwartz HS, Devin CJ, et al. Cost-utility of osteoarticular allograft versus endoprosthetic reconstruction for primary bone sarcoma of the knee: A markov analysis. Surg Oncol 2017; 115: 257–65.
6. van de Sande MAJ, Dijkstra PDS, Taminiau AHM. Proximal humerus reconstruction after tumor resection: biological versus endoprosthetic reconstruction. Int Orthop 2011; 35: 1375-80.
7. Grobet CE, Glanzmann MC, Eichler K. Cost-utility analysis of total shoulder arthroplasty: a prospective health economic study using real-world data. J Shoulder Elbow Surg 2021; 30: 1998-2006.
8. Losina E, Walensky RP, Kessler CL. Cost-effectiveness of total knee arthroplasty in the United States: Patient risk and hospital volume. Arch Intern Med 2009; 169: 1113–21.
9. Gundle KR, Cizik AM, Punt SE, Conrad EU, Davidson DJ. Validation of the SF -6D health state utilities measure in lower extremity sarcoma. Sarcoma 2014; 2014(450902): 1-4. https://doi.org/10.1155/2014/450902
10. Pattanaphesaj J. Health-related quality of life measure (EQ-5D-5L): measurement property testing and its preference-based score in Thai population [Doctoral dissertation]: Mahidol University; 2014. Available from https://www.hitap.net/wp-content/uploads/2016/11/EQ5D_thesis_final-copy.compressed.pdf
11. NESDC Economic Report 15th August 2022; Office of the Economic and Social Development Council, Thailand. Available from https://www.nesdc.go.th/nesdb_en/article_attach/article_file_20220830093238.pdf