



Original article

Rate of effect of surgical margins after breast conserving surgery and estimation of direct costs

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ARTICLE INFO

Article history:

Received 9 June 2021

Accepted 13 July 2021

Available online 16 July 2022

Keywords:

Breast cancer

Positive margins

Reexcision

Reoperation cost

Mastectomy

A B S T R A C T

Objective: Assessment of the reoperation rate in patients with positive resection margins after initial breast-conserving surgery for breast cancer and estimation of the cost to the hospital.

Method: 146 patients with diagnosis of invasive breast cancer were included, who were initially intervened with conservative surgery by the Gynecology and Obstetrics Service of Hospital Universitario de Tarragona Joan XXIII (HUTJ23) during the years 2018 and 2019. We calculated the rate of involvement of the surgical margins of the resection piece after initial conservative surgery, establishing in which cases it was necessary to carry out a second resection, estimating the added direct costs of the second surgical procedure, and comparing them with the costs established by the Catalan Health Service according to the level of the hospital and the Diagnosis-Related Groups (DRG) established by the National Health System.

Results: The rate of positive margins after initial conservative surgery was 20.55% and 19.17% patients underwent reoperation, generating a total expense of € 129,696.89, € 82,654.34 in conservative surgeries (€ 3757.01 on average per patient) and € 47,042.55 in mastectomies (€ 6720.36 on average per patient).

Conclusions: Margin involvement after breast-conserving surgery is synonymous for reoperation, this involves a series of direct costs. It is advisable to control the factors related to affected margins to minimize their impact.

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Tasa de afectación de los márgenes quirúrgicos tras la cirugía conservadora de mama y estimación de los costes directos

RESUMEN

Palabras clave:

Cáncer de mama
Márgenes positivos
Reintervención quirúrgica
Coste por reintervención
Mastectomía

Objetivo: Valoración de la tasa de reintervención en pacientes con márgenes de resección positivos tras cirugía conservadora inicial por cáncer de mama y estimación del coste para el hospital.

Métodos: Estudio observacional de la tasa de afectación de los márgenes quirúrgicos de la pieza de resección tras la cirugía conservadora inicial en mujeres con carcinoma de mama invasor durante los años 2018–2019 en el H. U. de Tarragona Joan XXIII (HUTJ23), estableciendo en qué casos fue precisa la realización de una segunda intervención sobre la mama. Se estiman los costes directos añadidos que supone el segundo procedimiento quirúrgico y se compara con el gasto según los pesos establecidos por el Servicio Catalán de Salud según el nivel del hospital y los Grupos Relacionados por el Diagnóstico (GRD) fijados por el Sistema Nacional de Salud.

Resultados: Se incluyó a 146 pacientes con diagnóstico de cáncer de mama invasor. Encontramos márgenes positivos tras la cirugía conservadora inicial en el 20,55% de los casos. Se reintervino al 19,17% del total de pacientes, generando las reintervenciones un coste de 129.696,089€, siendo 82.654,34€ para cirugía conservadora (3.757,01€ de media por paciente) y de 47.042,55€ en las mastectomías (6.720,36€ de media por paciente).

Conclusiones: La afectación de los márgenes tras cirugía conservadora de la mama es sinónimo de reintervención, lo que supone una serie de costes directos que dependen del tipo de cirugía y el régimen escogido (ambulatoria u hospitalizada). Es recomendable controlar los factores que inciden en los márgenes afectos para minimizar su impacto.

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Introduction

In many cases, and whenever possible, the treatment of choice for breast cancer is breast-conserving surgery (BC). It is accepted that mastectomy is equivalent to breast-conserving treatment with adjuvant radiotherapy in stages I and II, and no significant differences have been found with respect to survival.^{1,2} The aim of surgery is to remove the tumour with free margins,^{3,4} since the involvement of resection margins by residual tumour is directly related to the occurrence of local recurrence.⁵ Therefore, reintervention in the form of enlargement of the affected margins or mastectomy is almost imperative in these cases.

Healthcare managers use Diagnosis Related Groups (DRGs) to understand the consumption of healthcare resources associated with each procedure. DRGs use demographic and diagnostic variables to classify patients into clinically comparable groups according to length of stay in hospital and consumption of similar resources. The National Health System (NHS) establishes these DRGs and assigns a certain economic weight to each one, which is used as a payment system as well as for budgeting purposes. Based on these records, the cost of breast cancer reintervention at the Hospital Universitario de Tarragona Joan XXIII (HUTJ23) was estimated.

The aim of this study is to calculate the reintervention rate in patients with positive resection margins after initial breast-conserving cancer surgery and to estimate the cost to the hospital.

Methods

We conducted a descriptive observational study of breast cancer surgeries performed between 1st January 2018 and 31st December 2019 by the gynaecology and obstetrics department of the HUTJ23. In the group that underwent conservative surgery for infiltrating breast cancer, the clinical and anatomopathological characteristics of the tumour were analysed, as well as the status of the margins and reinterventions.

Patient duplications, patients with mastectomy as initial surgery, patients with an exclusive diagnosis of carcinoma in situ and patients in whom the lumpectomy revealed a complete response to chemotherapy and no residual tumour was found after neoadjuvant treatment were excluded.

The collection of clinical information was: hormonal status of the patients, anatomopathological characteristics of the tumours (size, lymphovascular involvement, histological grade and molecular subtype), status of the surgical margins, type of intervention and hospitalisation regime. This was done retrospectively from medical records and anatomical pathology reports of the resection specimens.

The prices and costs of the different medical and surgical procedures were obtained from the 2017 State Standard for DRGs, created by the Spanish NHS,⁶ and from the public prices established by the Catalan Health Service in 2013.⁷

When determining the cost of a procedure, the level or cluster to which the hospital belongs was established according to the hospital's equipment, range of services, activity, complexity and teaching intensity. HUTJ23 has 383

Table 1 – Average cost per unit (mean 4 levels established by the NHS).

INDICATOR	COST (€/day)
Conventional inpatient stay in Group 3 hospitals	704
Group 3 special care unit stay	749
Major outpatient surgery stay	634.70
Mastectomy procedures group 3	4554.89
Surgical procedures on breast except mastectomy group 3	3107.67
Plastic procedures of skin and subcutaneous breast tissue	2622.92
Breast prostheses	660

beds, 36 services and 57 MIR (Medical Intern Resident) positions, corresponding to a hospital in cluster or group 3.^{8,9}

In the DRG classification system, the costs of mastectomy, other breast surgery and medical treatment of malignant breast diseases are subdivided according to the severity of the disease, establishing four levels. For simplicity, [Table 1](#) shows the arithmetic mean cost for the four levels in each case.

To assess the economic impact of a surgical reintervention in breast cancer, the DRG corresponding to “breast procedures except mastectomy” (Procedure [ICD-9CM V2008] 85.20 and 85.23: partial excision of mammary gland) was taken, as there is no specific DRG. If there was a specific surgical DRG for “mastectomy” (85.33, 85.36 and 85.4: total mastectomy), this was the one used.

The study was approved by the centre’s Research ethics Committee.

Results

A total of 204 women underwent surgery for breast cancer during the period from 1st January 2018 to 31st December 2019 by the Gynaecology and Obstetrics Service of the HUTJ23. 146 conservative surgeries (71.57%) and 58 mastectomies (28.43%) were performed. [Table 2](#) specifies palpable and non-palpable cases, as well as the marking method used for non-palpable cases (harpoon or technetium).

Table 2 – Type of tumour in relation to surgery performed in the total number of patients.

	Palpable (%)	Non palpable (%)	Total (%)
Mastectomy	38	20 (technetium)	58 (28.43)
Conservative	70	76 (11 harpoon, 65 technetium)	146 (71.57)
	108 (52.95)	96 (47.05)	204

Table 3 – Patients with affected margins according to surgery performed.

		2018	2019	2018–2019 (%)
Lumpectomy	Free margins	42	52	94 (64.38)
	Affected margins	12	15	27(18.49)
Oncoplastic remodelling	Free margins	8	14	22 (15.06)
	Affected margins	0	3	3(2.05)
Total		62	84	146

Table 4 – Reoperated patients.

	Reoperated patients (%)
After lumpectomy	25 (17.12)
After oncoplastic remodelling	3 (2.05)
Total of reoperated patients	28 (19.17)
Total reinterventions	29*

* One patient was reoperated on two occasions.

During the period under study, 204 surgeries were performed for breast cancer with a rate of conservative surgery of 64% in 2018 and 62.4% in 2019.

[Table 3](#) shows the number and proportion of patients with affected margins according to the type of BC surgery performed. In the 146 conservative surgeries, free margins were obtained in 116 of them (79.45%), while the remaining 30 cases showed marginal involvement of the tumour (20.55%). Of the 30 cases with affected margins, 8 were reported as having carcinoma in situ at the margin (26.6%), 6 were complete responses after initial neoadjuvant imaging (20%), which had residual carcinoma at the affected margin and 16 cases had invasive carcinoma involvement (53.4%). Of the 30 cases with positive margins, 28 patients were re-intervened, i.e., 19.17% of the total number of those operated on conservatively. Twenty-two patients underwent a second conservative surgery, while six underwent mastectomy as salvage surgery. One patient who underwent conservative surgery on both occasions required a third operation in the form of a mastectomy due to persistently positive margins after the second conservative surgery. Thus, 28 patients underwent further surgery, but the number of reoperations carried out was 29.

In two cases with affected margins (1.36%), reoperation was discouraged. One case was a woman with a 0.9 cm G1 infiltrating ductal carcinoma (IDC) G1 whose outer margin was in contact with the skin. Another case was an 87-year-old woman with Alzheimer’s disease in whom the delayed anatomical pathology study showed that the carcinoma affected one of the resection margins, and it was decided not to perform a second surgery due to her comorbidities.

The number and proportion of reoperations, according to the initial surgery performed, are specified in [Table 4](#).

Table 5 – Cost per patient according to type of reoperation and hospitalisation.

Type of intervention (cost in €)	Type of hospital stay (cost in €)	Number of patients	Days of stay (∑ patients)	Total cost (€)
Enlargement with BC 3107.67	MOS	18		67,362.66
	634.70			
	Hospital stay	3	3	11,435.01
	704			
	SCU	1	1	3,856.67
	749			
Enlargement with mastectomy 4554.89	MOS	2		10,379.18
	634.70			
	Hospital stay	2	7	14,037.78
	704			
	SCU	2	2	10,607.78
	749			
Enlargement with mastectomy 4554.89	Hospital stay	1	5	12,017.81
+				
IBR (latissimus dorsi flap + breast prosthesis) 3942.92				
				129,696.89

BC: Breast-conserving surgery; IBR: Immediate Breast Reconstruction; MOS: Major Outpatient Surgery; SCU: Special Care Unit.

36.7% of the women with affected margins were premenopausal (11/30 women). Regarding the anatomopathological characteristics of the tumours analysed in the group with affected margins, 12/30 (40%) cases had tumours larger than 2 cm, 7/30 (23.4%) cases had lymphovascular invasion, 21/30 (70%) cases were G2-G3 and 4/30 (13.4%) cases were HER-2 positive with negative hormone receptors, and 5/30 (16.7%) cases were triple negative.

Most of the re-interventions were performed in Major Outpatient Surgery (MOS), which is less expensive than conventional hospitalisation or Special Care Units (SCU). The cost of additional procedures required by individual patients, immediate breast reconstruction with flap and/or placement of breast prostheses, tissue expanders or lipotransfer, is also considered, as can be seen in the variables specified in Table 5.

It is estimated that the cost of the 29 reinterventions for positive margins for the period 2018–2019 was € 129,696.89 with € 82,654.34 being for BC surgery, with an average of € 3757.01 per patient and € 47,042.55 for mastectomies with an average per patient of € 6720.36.

Discussion

Breast cancer is the most common cancer in women and the leading cause of neoplastic death in this population. BC surgery has become the treatment of choice for the control of loco-regional disease.^{1,2} Unfortunately, in some BC surgery, free margins are not achieved in the first intervention and these women must undergo subsequent surgeries to increase the resection margin.

The rate of affected margins obtained in our study, 20.55% after initial conservative surgery, is within the limits published in the literature. Haloua et al.¹⁰ collected data from 9276 patients through the Dutch National Network, obtaining a positive margin rate of 16.4% after surgery for invasive and in

situ breast cancer. In a recent cohort study, based on population-based data from the Dutch Pathology Register, van Deurzen¹¹ reported a 16.9% rate of affected surgical margins. Langhans et al.,¹² with a series of 4118 patients with pre-surgical localisation by metal harpoon, reported a reoperation rate for affected margins of 17.6%. Closer to our rate is the rate reported by Laws et al.,¹³ with an overall rate of 20.8% in a series of 1165 patients in Canada. We also found publications where the rate is higher than ours, varying between 19% and 34% depending on whether the surgery applied was a traditional BC technique or oncoplastic surgery.^{14–16}

Second surgeries obviously increase the cost of the overall treatment of breast cancer. In our study it was only possible to estimate the cost of hospital care related to the new surgery, but it should be remembered that there are also indirect and intangible costs related to this process that have not been measured and which are estimated to be 5% more in cost over the total value.¹⁷ It should be borne in mind that the cost of BC variants is not applicable to all patients equally, as the expense differs considerably whether lumpectomy or oncoplastic remodelling is performed, the latter requiring longer surgery time and a more complex technique. The problem lies in the fact that the Spanish NHS does not have specific DRG codes for each different procedure in conservative treatment, so there may be discrepancies between results and reality.

It is worth highlighting a study published by Angulo-Pueyo¹⁸ which analyses the population variability of surgical treatment of breast cancer, both inpatient and outpatient, using conservative surgery plus radiotherapy and non-conservative surgery, and estimates the opportunity cost associated with the use of one or the other. This study publishes that, according to RECH (Spanish Hospital Costs Network), the average cost of conservative surgery was €7078, and that of non-conservative surgery was €6161. According to DRG, an overall average cost of €5977 and €8526 was obtained for conservative and non-conservative surgery, respectively.¹⁸

According to these data, the results of our study show that the costs of surgery would be lower, with an average of €3757.01 per patient for BC surgery and €6720.36 for mastectomy. Bearing in mind that in our study we are talking about re-interventions, this is an added cost to the initial treatment. Even so, transferring the data to the first surgery and not to the reintervention, we believe that the difference may lie in the strict regime of outpatient surgery and early discharge that is applied in our department.

In other countries, Pataky & Baliski¹⁶ calculated the cost in Canadian dollars of surgical reoperation after initial BC surgery in the city of Kelowna (Canada): \$2941 for conservative surgery (\$8225 including radiotherapy) and from \$4232 to \$8160 for mastectomy, depending on whether or not immediate breast reconstruction was performed. In the United States, re-operating patients after initial BC surgery increased hospital costs by \$11,621 for BC and \$26,276 for mastectomy during the first two years after diagnosis, with an average of \$16,072 for each additional surgery.¹⁹

It is difficult to define the overall cost (surgery and adjuvant treatments) of treating a patient diagnosed with breast cancer in Spain, as no recent studies have been carried out at the national level on how much treatment costs per patient. In 2006, Lorente et al.¹⁷ carried out a study for the Ministry of Health that sought to measure the direct and indirect costs of the four most prevalent types of cancer in Spain, including breast cancer. The total costs of the disease amounted to 325 million euros for the whole of Spain, with more than 50 million euros in Catalonia alone.

In the literature we find several studies that analyse the overall costs of treatment according to stage. Corral et al.,²⁰ in Catalonia (2009), Arrospe et al. in 2015⁹ in the Basque Country (2015) and recently a systematic review concluded that the more advanced the stage, the higher the resource consumption, being 32%, 95% and 109% higher in stages II, III and IV respectively, compared with stage I.²¹

If only the surgical procedure is taken into account, the average cost of mastectomy is higher than that of BC, but to consider BC as a complete local treatment, subsequent radiotherapy is necessary. According to information obtained from the Hospital del Mar in Barcelona, in general, radiotherapy generates an average additional cost of €3062 for BC.²⁰ In this study, it was beyond our objectives to assess the cost of radiotherapy, but it is important to note that the cost of conservative treatment increases considerably if it is associated with radiotherapy, and may even be equal to or greater than that of mastectomy.

One of the objectives of cost estimation studies on a disease is to serve as a measure of the benefits of prevention programmes. Investing in strategies, before or during the first surgery that avoid a second surgical procedure can lead to savings, not only for the hospital, but mainly to improved patient satisfaction.

There are some factors that contribute to the rate of reoperation where action is difficult, such as tumour size greater than 2 cm, intermediate and high histological grades, lymphovascular invasion, presence of ductal carcinoma in situ, multifocality, being aged under 60 years¹⁸ and tumours with lobular carcinoma histology.²² But there are other factors that contribute to the risk of affected margins on which some

strategies can be implemented. Intraoperative pathology study of the surgical specimen has been shown to decrease the percentage of patients requiring a second operation compared to delayed study of the specimen.²³ This factor depends on the availability of the healthcare centre and implies a higher cost for the surgical procedure, but a saving in reoperations. In our centre, margins were analysed intraoperatively in all cases. If, of the women with affected margins (n = 30), we exclude the final cases of carcinoma in situ by pathology (8 cases) and the complete responses by imaging after neoadjuvant treatment that later resulted in residual tumour at the margin (6 cases), we are left with only 16 cases of invasive carcinoma as a margin for improvement.

Another strategy that may decrease the rate of positive margins is routine shaving of the cavity margins (additional tissue circumferentially around the cavity left by the lumpectomy).²⁴

Some authors use the technique of ultrasound-guided resection based on tumour assessment before and during surgery, as well as of the resected specimen. It seems that this technique could considerably reduce the rate of affected margins, but it must be borne in mind that ultrasound is not the ideal technique for assessing microcalcifications and, therefore, its use is not generalisable, although it could be useful in centres with availability and experience.²⁵

In the case of non-palpable in situ breast cancer, the challenge is for the whole team: the surgeons depend on the marking of the tumour and their experience in removing a tumour they can neither see nor touch. The radiologist/nuclear physician must master the marking techniques and the pathologist's difficulties are multiplied. A study carried out by our group *grupo*²⁶ states that the ROLL technique, compared with the harpoon, does not generate significant differences in terms of margin involvement. The only drawback found is that its cost is higher than that of the harpoon. Therefore, it is vitally important to promote the learning curve of healthcare professionals in the chosen technique in order to reduce the incidence of positive margins and reinterventions.²⁷

Depending on the type of initial surgery performed, there are several studies that support the superiority of oncoplastic surgery over lumpectomy,^{13,14} based on a lower rate of affected margins, a lower percentage of reoperations and a lower incidence of local recurrence, with no differences in survival. This is demonstrated in our study, with the rate of reoperation in the oncoplastic surgery group being much lower than in conventional BC. In general, it requires more surgery and anaesthesia time than other BC techniques, but it is still a more cost-effective option than lumpectomy in the appropriate patient.^{13,18}

There are some biases to note in our study. Note that the costs of reinterventions refer to the years 2018 and 2019, but the healthcare resource utilisation data come from a combination of 2013 and 2017 sources. Thus, it is likely that there is a deviation in the final cost results, expected to be underestimated, due to the increasing trend in the price of health services.

It would have been desirable to have more data to be able to estimate also the indirect costs (lost labour production by patients, lost labour production by caregivers, lost leisure

time, etc.) generated by breast cancer reinterventions in order to have a real understanding of the problem posed by a second surgery.

Conclusions

In patients with positive margins, a second surgery is mandatory, which entails direct costs for the hospital, indirect costs and intangible costs in the form of a deterioration in quality of life.

The various conservative surgical procedures are incompletely recorded in the Spanish health care system. It would be desirable to update these registers in order to make a true estimate of the cost.

Strategies to reduce the rate of reoperation include improving the resources allocated to intraoperative assessment of the surgical specimen, as well as improving surgical techniques.

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