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ORIGINAL ARTICLE

Effect of harmonic scalpel on seroma formation following surgery for breast cancer: a prospective randomized study

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Summary

Purpose: *With the escalating cost of healthcare provision, surgical techniques that could lead to shorter postoperative stay and reducing cost of health provision are welcomed. We report the results of a prospective randomized trial to investigate the role of harmonic scalpel (HS) in reducing postsurgical seroma formation, complications, pain and consequent cost in breast surgery.*

Patients and methods: *Thirty-three procedures were carried out on 32 women. Patients were prospectively randomized to either HS or electrocautery (EC). The two cohorts were accordingly matched and postsurgical seroma volumes, complications and pain scores were documented.*

Results: *There were 16 procedures in the HS and 17 in the EC group. First 48h drainage, total drained volume, aspirated volume, operative time, pain score, number of patients that developed seromas, number of clinic visits for aspiration, complications and required analgesia were comparable in the two groups. Multivariate analysis showed no significant correlation between the total amount of seroma drainage and the known risk factors (body mass index/BMI, size of the invasive tumor and number of positive nodes).*

Conclusion: *No significant reduction in seroma formation or wound complications and pain could be found with the use of HS. We were unable to demonstrate any significant clinical advantages with the use of HS or cost benefit.*

Key words: breast surgery, complications, cost, harmonic scalpel, pain

Introduction

Despite the gaining popularity of breast-conserving surgery and sentinel lymph node biopsy in the treatment of breast cancer, there will always be a subgroup of patients needing a more radical surgery (mastectomy and/or axillary lymph node clearance) that requires longer hospital stay and more intense postoperative follow up. However, with the escalating cost of health provision and budgets stretched to almost breaking point, any surgical techniques that could shorten the postsurgical length of hospital stay and/or reduce the need for medical assistance and thereby reduce expenditure would be of considerable value.

Although seroma formation can be regarded as more of a nuisance rather than a complication, it is a frequent reason for repeat postoperative clinic visits, it can trigger further complications and, of course, usually necessitates the placement of suction drains intraoperatively. This clearly not only increases the patients' discomfort but also leads to an additional costly medical assistance.

The exact etiology of seroma formation is unclear. Biochemical analyses have shown that it contains substances which are normally present in inflammatory exudates [1]. This in principle implies that surgical techniques which minimize tissue damage would theoretically reduce the inflammatory exudates and the seroma formation. Surgery performed with conventional electrocautery has been associated with increased morbidity [2,3], which was attributed to collateral tissue trauma.

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Based on initial reports that causes less thermal injury, HS is investigated here as a method to reduce seroma formation and the need for protracted postoperative care. Other complications are also looked at and cost-effectiveness analysis is performed.

Patients and methods

This study was powered to detect a 40% reduction in total seroma drainage volume. In keeping with routine practice this could have translated to a cost benefit of 2 days less of hospital stay, should we were able to demonstrate a reduction in drain volumes using HS.

After obtaining local ethics committee approval and informed consent, 32 women with a median age of 57 years (range 32-86) requiring 33 surgical procedures were prospectively randomized to HS or EC surgery. The study population consisted of women requiring surgery for either primary *in situ* or invasive breast carcinoma or a prophylactic mastectomy. The procedures included modified radical mastectomy, simple mastectomy with sentinel node biopsy, skin sparing mastectomy with immediate reconstruction and wide excision and axillary clearance as a part of breast-conserving surgery. Women whose immediate reconstruction included procedures other than a submuscular silicone implants were excluded from the study. Women on preoperative anticoagulant therapy were also included in the study. All 33 procedures were carried out on the Hedley Atkins Unit, Guy's Hospital, between May and December 2005 by the same two experienced full time breast surgeons. Randomization was obtained by drawing sealed envelopes prior to surgery.

The EC procedures were carried out using a Valleylab Force FX^{TM} (Tyco Healthcare, Valleylab Force FX), at a power setting of coagulation of 30 with a spatula diathermy tip and routine monopolar diathermy forceps. In the second group we used an Ethicon Endosurgery Ultracision^{TM} HS with a curved blade or hook as the dissecting tool at the end of the hand-piece and power setting of 5 for dissection and 3 for heamostasis. The intercostal perforators were coagulated with EC in both groups and axillary clearance included level III.

Patients that underwent an axillary clearance had a closed suction drain system (Redon) (10 fr) left *in situ* and this was connected to a closed negative pressure drainage bottle. Those that underwent a modified radical mastectomy had two such drains *in situ*, one in the axilla and another below the lower mastectomy skin flap. These drains were removed in all patients when the drain volume fell to less than 100 ml/24 h or 5th postoperative day, whichever occurred first. The exception to this rule was patients who had immediate prosthetic reconstruction where the drains were removed when the drain volume fell to less than 30 ml/24 h. All drain volumes were recorded on the ward as well as in the subsequent clinic visits that the patients attended after discharge.

In addition to seroma formation we also recorded the postoperative pain experienced by patients. The pain scores were recorded on each day until discharge using the VAS (visual analogue scale scoring system). The pain scores, ranging between 0 and 10, were then compared between the 2 groups. In addition, we recorded the amount of postoperative analgesia required by the study population. Patients were divided into 5 groups: group 1, no analgesics; group 2 paracetamol only; group 3 paracetamol plus another analgesic for up to 3 days; group 4 paracetamol plus another analgesic for more than 3 days; subgroup 5 paracetamol plus 2 other necessary analgesics (Table 1).

We also recorded other relevant data such as BMI, anticoagulant treatment, size of primary tumor, nodes recovered/nodes involved, operative time, daily drainage, complications such as skin necrosis, haematoma or infections.

Statistical methods

Standard two-sample t-test was used for the statistical comparison of the two groups (age, BMI, nodes resected and involved and tumor size) and x^2 test for the comparison of the type of surgical procedure performed.

Multivariate analysis was used to investigate potential correlations between the total amount of drainage and BMI, size of the invasive tumor and number of positive and removed nodes.

Table 1. Analgesics required after electrocautery or harmonic scalpel surgery

Method	*No analgesics*	*One analgesic*	*Two analgesics*[a]	*Two analgesics*[b]	*Three analgesics*
Electrocautery	1	5	8	3	0
Harmonic scalpel	0	6	3	2	3

[a]Paracetamol plus another analgesic (ibuprofen or codeine). Second analgesic for up to 3 days; [b]Paracetamol plus another analgesic (ibuprofen or codeine). Second analgesic for more than 3 days.
One patient with the bilateral procedure (HS group) was excluded from this Table

Standard two-sample t-test was used for the statistical comparison of the end points of the two groups (48 h drainage, total drainage, aspirated volume, number of clinic visits for seroma aspirations, grand total volume, operating time, pain score, and number of operations complicated with seroma formation).

x^2 test was used to compare the wound complications and the required analgesics.

Results

Seventeen patients underwent 17 procedures in the EC group and 15 patients had 16 procedures in the HS group. The two groups were matched for age, BMI, size of invasive tumor, nodes recovered and type of procedures. There was a difference in the number of recovered nodes with a larger number removed in EC group. This may be due to the fact that in EC group there was only 1 patient who did not have an axillary nodal clearance as compared to 4 patients in the HS group, although this difference was not statistically significant. The characteristics of the patients, their tumors and the types of the surgical procedures are summarized in Table 2. Surgical procedures are listed in Table 3.

Regarding the study end-points, no difference was found between the two groups (Table 4) in the first 48 h drainage, total drained volume, total aspirated volume, operative time, pain score, number of patients that developed seromas, number of clinic visits for aspiration or number of complications. Of the 33 patients, 2 had postoperative bleeding (one in each group) and were excluded from the calculation of the seroma drainage and aspiration. Similarly, of the total 33 patients, one who had a bilateral procedure (HS group) was excluded from the pain and needed analgesia comparison.

In the multivariate analysis no significant correlations between the total amount of drainage and the known risk factors, such as age, BMI, size of the invasive tumor, number of positive or removed nodes were found.

Table 3. Types of procedures in electrocautery and harmonic scalpel groups

Procedure	*Electrocautery*	*Harmonic scalpel*
MRM	11	8
WLE + ANC	4	4
ANC alone	1	0
SM	0	1
SM + SNB	1	0
SSM + Implant	0	2
SSM + SNB + Implant	0	1

MRM: modified radical mastectomy, WLE: wide local excision, ANC: axillary node clearance, SM: simple mastectomy, SNB: sentinel node biopsy, SSM: skin sparing mastectomy

Similarly, wound complications were not statistically different between the two groups but there was a trend towards fewer complications in the HS group (Table 5). There was 1 case of haematoma in each group and 2 cases of surgical infections and 1 case of skin necrosis in the EC group.

No difference in the pain score was found between the two groups. Overall mean value of pain scores were 9 and 11.8 for the EC and the HS group, respectively. Similarly, no differences in the required analgesics between the groups were found (x^2 7.78, p=0.1, Fischer's exact test=0.1006; Tables 1 and 4).

Discussion

Seroma: the problem

The substantially high incidence of seroma formation after breast surgery is well documented in the

Table 2. Main characteristics of patients, tumors and procedures of electrocautery and harmonic scalpel groups

Variable	*EC mean (range)*	*HS mean (range)*	*p-value*	*Difference*
Age (years)	60 (40-76)	58 (32-86)	0.6	NS
BMI	25.63 (21.29-3.95)	23.96 (18.75-3.3)	0.2	NS
Nodes involved	4.75 (0-36)	0.9333 (0-4)	0.1	NS
Size of invasive tumor (mm)	24.53 (0-80)	22.02 (0-75)	0.7	NS
Nodes recovered	18.82 (4-42)	12.13 (0-26)	0.0344	Significant
MRM (pts/total)	11/17	8/16	0.6	NS
ANC (pts/total)	5/17	4/16	0.9	NS
Other (pts/total)	1/17	4/16	0.29	NS

EC: electrocautery, HS: harmonic scalpel, BMI: body mass index, MRM: modified radical mastectomy, ANC: axillary node clearance, NS: non significant

Table 4. Results after electrocautery or harmonic scalpel breast surgery

Variable	*EC mean (range)*	*HS mean (range)*	*p-value*	*Statistical significance*
Drainage 1st 48h (ml)[a]*	409.7 (180-770)	418 (110-730)	0.9	NS
Drainage (ml)[b]*	896.3 (280-2115)	683.7 (190-1390)	0.4	NS
Aspirated vol (ml)[c]*	384.1 (0-1710)	406.3 (0-1540)	0.9	NS
Grand total vol (ml)[d]*	1280 (280-3075)	1090 (190-2260)	0.5	NS
Op time (min)[e]	63.06 (45-95)	72.27 (40-90)	0.1	NS
Pain score[f]**	9	11.8	0.2	NS
Number of procedures with seromas after removing the drains[g]*	12/16	11/15	0.7	NS
Clinic visits[h]*	2.3	2.25	0.9	NS

EC: electrocautery, HS: harmonic scalpel, a: Drainage 48h: total drainage in the first 48h (ml), b: Drainage: total drainage before removal of drains (ml), c: Aspirated vol: total volume of aspirated fluid after removal of drains (ml), d: Grand total vol: drainage plus aspirated volume (ml), e: Op time: operative time in minutes ("skin to skin"), f: Pain score: mean value of the pain scores of the first 4 postoperative days added, g: Procedures with seromas after removing the drains: number of procedures that were complicated with seroma formation after removing the drains, h: Clinic visits: mean number of clinic visits necessary for seroma aspiration

*of the 33 procedures, 2 that developed haematomas (1 modified radical mastectomy in each group) were excluded

**of the 33 procedures 1 patient with bilateral procedures (HS group) was excluded

world literature and it is reported as high as 60% [4-11]. Although not life-threatening, seromas are responsible for significantly further morbidity and need for prolonged postoperative care. Seroma can be associated with, pain, delayed wound healing, wound dehiscence, infection, prolonged hospitalization, decreased limb mobility, arm swelling, flap necrosis, reoperation, lymphoedema, increased numbers of postoperative clinic visits for aspiration, psychological morbidity and they can consequently increase the overall cost of health care provision [12-14]. Potential delay of the start of adjuvant treatment (chemo- or radiotherapy) has also been reported [4,15,16].

A number of methods have been proposed to eliminate seroma formation, such as suturing flaps, mechanical pressure, use of fibrin sealant, restriction of shoulder movement, closed wound drainage, use of different number of drains or use of varying degree of suction pressure. Early drain removal, no placement of drains at all or discharge of the patients with drains *in situ,* have been considered to reduce patients' hospital stay. In a systematic review of these methods none of them were found to provide a solution to the problem [17].

HS has emerged as an alternative surgical tool for dissection and haemostasis, especially in the field of minimally invasive surgery. Several recent studies have suggested that ultrasonic energy is able to reduce seroma formation rates [18,19]. The current prospective randomized controlled study was designed to evaluate the ultrasonic energy dissection technique in breast surgery and its effect on seroma formation, pain level and overall cost.

Table 5. Postoperative complications after electrocautery or harmonic scalpel breast surgery

	Haematoma n (%)	*Infection n (%)*	*Skin necrosis n (%)*	*Total number of complications n (%)*
Electrocautery	1 (5.9)	2 (11.8)	1 (5.9)	4 (23.5)
Harmonic scalpel	1 (6.2)	0	0	1 (6.2)

Background: Electrocautery and Harmonic scalpel

EC has been widely used in breast surgery. There is a growing body of evidence indicating that it could be responsible in part for various complications. Recent studies have shown that cautery-associated thermal injury causes damage of subdermal vascular plexus and incomplete occlusion of vascular and lymphatic channels [18,20,21]. Diathermy may fail to adequately seal the lymphatics as well as cause more surrounding collateral tissue damage. Porter et al. have also shown that use of EC increases the rate of seroma formation [20].

Ultrasonic energy however, causes a breakage of hydrogen bonds and the formation of denatured pro-

tein coagulum. This coagulum seals off the vessels and lymphatics, resulting in decreased lymphatic drainage. Lateral thermal injury has been shown to be halved with the HS as compared to EC in animal models [22]. As thermal injury can compromise the viability of the tissue and create local conditions that may favor bacterial growth, HS can potentially decrease the flap necrosis and infection rates. Moreover, because of less lateral tissue disturbance, it might be able to reduce the exudate produced and consequently reduce the seroma formation. There are a small number of studies in the literature comparing EC and ultrasonic energy in breast surgery [18,19,23-26], and the number of prospective randomized trials is even smaller (Table 6).

Volume of drained fluid

Ultrasonic dissection has been reported to reduce the amount of drained fluid in at least 2 prospective randomized studies [18,19]. In both of these studies the difference resulted in decreased number of days with drains. Another prospective randomized study found no difference between the HS group and the scissors plus EC group [23] (Table 6). In the recent study of Adwani et al. no statistically significant difference either was found between HS and sharp dissection groups [27].

The present study demonstrated a lack of significant difference in the amount of the drained fluid between the groups investigated (EC and HS): a total postoperative mean seroma volume of 896.3 ml (range 280-2115) in the EC group vs. 683.7 ml (range 190-1390) in the HS group. However, since our study was designed to detect a difference of 40% or more, it may be explicable why this difference (which is approximately 23.7%) did not reach significance.

Seroma and aspirated volume

Post-discharge seroma formation is the result of the continuous fluid accumulation after the removal

Table 6. Prospective randomized trials of harmonic scalpel vs. electrocautery for breast surgery

Study	*Deo 2002*	*Galatius 2003*	*Lumachi 2004*	*Present study*
Groups (number of patients)	EC: 23 HS: 23	EC: 29 HS: 30	EC: 47 HS: 45	EC: 17 HS: 16
Type of operation	MRM with level I, II or III axillary dissection	MRM with level II axillary disection (but the axillary dissection with scissors in all cases)	Level II axillary dissection in MRM and BCS	MRM and BCS with level III axillary dissection, SM and SSM with implant ± SNB
Instrument	Harmonic scalpel	Harmonic scalpel	Ultrasonic scissors	Harmonic scalpel/hook
Operative time, min (range)	EC: 100±24 HS: 104±24	EC: 180 (120-260) HS: 190 (120-250)	–	EC: 69.4 (45-95) HS: 72.27 (40-90)
Drainage, ml (range)	**EC: 1085±690** **HS: 590±30**	EC: 585 (130-1455) HS: 645 (95-1570)	**EC: Increased** **HS: Decreased**	EC: 896.3 (280-2115)* HS: 683.7 (190-1390)*
Days with drains	**EC: 9±7** **HS: 5±**	–	**EC: Increased (by 20%)** **HS: Decreased (by 20%)**	–
Patients with seroma n/total	EC: 5/23 HS: 4/23	EC: 20/29 HS: 20/30	EC: 19/47 HS: 9/45	EC: 12/16* HS: 11/15*
Blood loss, ml (range)	**EC: 294±155** **HS: 60±35**	EC: 300 (100-790) HS: 300 (40-1200)	–	–
Punctures for aspiration, median (range)	–	EC: 1 (0-8) HS: 2 (0-20)	–	EC: 2 (0-7)* HS: 2 (0-7)*
Complications	EC: Nil HS: Nil	EC: 1 HS: 3	EC: Nil HS: Nil	EC: 4 HS: 1
Postoperative pain score (VAS)	–	–	–	EC: 9** HS: 11.8**

EC: electrocautery, HS: harmonic scalpel, MRM: modified radical mastectomy, BCS: breast conserving surgery, SM: simple mastectomy, SSM: skin sparing mastectomy, SNB: sentinel node biopsy, VAS: visual analogue scale
Statistically significant differences in **bold**
*one MRM patient in each group was excluded due to post-operative haematoma development
**one patient with bilateral procedures (HS group) was excluded from the pain score comparison

of the drains. Usually it is addressed with the puncturing and aspirating the clinically detectable seromas. In none of the randomized studies summarized in Table 6 the number of the patient with seroma formation was statistically different between the two groups. The rates varied from 22% to 70% for EC and from 17% to 69% for the HS group [18,19,23]. Similarly, no difference in the numbers of aspirations was found. Our higher rates of seroma in the whole study (EC: 70% and HS: 69%) could be attributed to the level of axillary clearance, which has always been level III, and possibly to the aggressive post-discharge aspiration of even relatively small seromas.

The average total volumes aspirated were also comparable between groups in the present study: 384.1 ml with 2.3 outpatient visits for the EC group and 406.3 ml with 2.25 in the HS group. Similarly, Adwani et al. report no difference in seroma volumes aspirated between HS and sharp dissection groups [27].

Non-controlled series present similar results. Only 1 out of 14 patients who had modified radical mastectomies with HS developed seroma [24]. After minimally invasive HS breast surgery seroma rate of 43% (13/30) was reported [26].

The incidence of seroma has also been shown to correlate with patients' age, breast size, BMI, hypertension, presence and number of malignant nodes in the axilla, previous surgical biopsy, drains and early shoulder exercise [17,28]. In most of the studies no definite correlation between number of resected nodes and seroma formation was found [17,19,29,30]. In our study the number of nodes recovered was higher in the EC group because of the higher number of axillary clearances in this group. However, this was not associated with significantly increased rate of seroma formation.

Operative time

Operative time is also of some significance as prolonged times may further burden a patient with comorbidities, increase the waiting list for surgery, as well as cost. A cost analysis at our institution estimates that theatre time cost up to £720/h which is by no means a small sum. It is suggested that operating time does not routinely increase with the use of a HS. Deo et al. [18] found no difference in the operating time of modified radical mastectomies with level I, II or III axillary node clearance between the conventional EC and HS groups (100±24 vs. 104±26 min). In another non-controlled study by the same group [24] a median operative time of 117 min was reported. Similarly, lack of significant difference was reported by Galatius et al. [23]. Lumachi et al. also demonstrated the same operative time in their HS study [19]. In a minimally invasive setting for upper outer quadrant lumpectomies with axillary node dissection Lim et al. [26] reported an average operative time of 37 min (range 30-48). In the present study no difference between groups could be detected either: 69.4 min for the EC vs. 72.27 min for the HS group.

Pain

Pain is always a substantial parameter to assess patient well being in the immediate postoperative period. To the best of our knowledge this is the first study to investigate the pain level after use of HS in breast surgery and no difference was found either in pain scores or the postoperative analgesia required (Tables 1 and 4).

Non-seroma complications

Complications other than seromas are encountered in breast surgery as well. These can be more severe and can similarly cause delay of further treatment, morbidity and increase the cost. The most common of these are skin necrosis, infection of the surgical site and bleeding [23].

In our series slightly more complications were encountered in the EC group. In the HS group only one young patient who was lactating around the time of surgery, with large vascular breasts, presented with a postoperative haematoma. In the EC group 4 complications were recorded. One patient who was on warfarin developed a postoperative haematoma that required evacuation. Two patients in this subgroup also developed infection of the surgical site that required antibiotic therapy and the last one developed superficial skin necrosis of the wound edge, which resolved satisfactorily with local care. These findings substantiate the theory that the less lateral thermal injury of the ultrasonic energy may account for these results [7,18,20-22].

However, other randomized studies have presented heterogeneous findings. No complications in either group were reported by Deo et al. and Lumachi et al. [18,19]. More complications were reported in the HS group by Galatius et al. [23]. In their study 1 haematoma, 1 case of wound infection and 1 wound necrosis occurred in the HS group vs. only 1 case of wound necrosis in the electrocautery/scissors group. Similarly, 3 (2 wound infections and 1 flap edge necrosis) vs. none complications were reported in the HS vs. sharp dissection groups, respectively, by Adwani et al. [27]. In another non-controlled study, only one case of paraesthesia after minimally invasive ultrasonic excision of the upper outer quadrant of the breast with axillary node clearance was reported [26]. Finally, no compli-

cations were observed in a non-controlled report of a series of 14 modified randomized mastectomies with HS by Deo and Shukla [24].

From a surgical viewpoint, the results of our study suggest that HS is at least as safe as EC in terms of postoperative complications. The way HS works could result in fewer side effects but this has as yet to be proven. Another issue that became quite evident early in this study is the lack of the typical "jumping" of the muscles when dissection is carried out close to muscles or nerves. This can make this particular phase of the operation more manageable but at the same time requires care not to injure the neurovascular bundles.

Cost

Cost benefit ratio is a tool widely used to evaluate new surgical procedures. Although there may be minor institutional procurement costs variance, the disposable active element of the HS is invariably more expensive than that for the EC. At our institution the HS blade costs £85 vs. £2.34 for a Teflon spatula used for the EC. Although not a negligible difference in a cost-conscious time, it can be easily offset by a reduction in the hospital stay. It is estimated that on average a patient's overnight stay costs the health service somewhere in the region of £650. Therefore, a reduction of the hospital stay by one day would offset the cost of HS blade. In the present study, no potential reduction in the hospital stay could be identified through the decrease of the volume drained; thus the higher cost of HS is not compensated by earlier discharge.

Conclusion

In our study there was no significant difference in the drained volume, the seroma formation or other complications, as set out beforehand. Despite a statistically non-significant reduction in seroma formation in HS arm that may have resulted in earlier discharge, the results of this study and others' suggest that it is unlikely that there is a significant clinical or surgical difference or any financial benefit between HS and conventional methods.

Surgical teams should make their own individual decisions on which techniques to employ, depending on their own practice in dealing with patients' early discharge.

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