Improved patient outcomes using the enhanced recovery pathway in breast microsurgical reconstruction: a UK experience

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Introduction: The enhanced recovery after surgery (ERAS) pathway is a protocol aimed at optimizing patient care by reducing the physiological alterations caused by surgery, thus reducing recovery time, surgical morbidities and length of stay. This study assessed the impact of ERAS on patients undergoing microsurgical breast reconstruction.

Methods: Patients undergoing microsurgical breast reconstruction over an eight-month period were retrospectively examined. LOS, complication rates and perioperative outcomes were analysed. Results were compared between patients admitted on the traditional recovery after surgery (TRAS) and the ERAS pathways.

Results: One hundred and thirty-eight patients were included. Seventy-two patients were admitted on the TRAS pathway and 66 patients on the ERAS pathway. There was no difference in median LOS (4 days) between the two groups, p = 0.48. We noted a significant reduction in the total number of major complications (ERAS 11%, TRAS 24% p = 0.04) as well as significant differences in time to catheter removal, time to independent mobilisation, total opioid usage and time to removal of PCA, all in favour of the ERAS group. There was a non-significant reduction in return to theatre.
Introduction

Enhanced recovery after surgery (ERAS) care pathways have gained popularity since their introduction in 1997 by Kehlet et al. They are systematic, standardised, evidence-based, interdisciplinary protocols that aim to improve surgical outcomes by reducing the post-operative stress response to surgery and limiting variations in perioperative care. ERAS pathways have been associated not only with reductions in hospital length of stay (LOS), readmissions and reoperations but also with reduced complication and morbidity rates. These clinical pathways are now widely adopted with high uptake in many surgical disciplines. Considering the emphasis that is currently placed on cost reduction and the transparency of surgical outcomes, ERAS pathways are of significant clinical value and can have important implications for healthcare systems. These pathways aim to improve outcomes by accelerating the post-operative convalescence period and decreasing costs whilst maintaining or improving quality of care. Despite evidence of multiple benefits of ERAS pathways, there is still limited experience for patients undergoing breast microsurgical reconstruction.

The aim of this study was to assess how the introduction of an ERAS pathway for patients undergoing microsurgical breast reconstruction affected surgical outcomes, complication rates and LOS, and compare these results to the previous traditional recovery after surgery (TRAS) perioperative care model in a tertiary plastic surgery unit.

Patients and Methods

Study design

This cohort study was a retrospective review of perioperative data of consecutive patients undergoing microsurgical breast reconstruction for breast cancer over an eight-month period at Queen Victoria Hospital, East Grinstead. The study was approved by the local research committee and the manuscript prepared in accordance with STROBE guidelines. All consecutive patients over a four-month period (May to August 2015) when the ERAS pathway was introduced were compared to the preceding four-month period (January to April 2015), a control group of consecutive patients who underwent microsurgical breast reconstruction using TRAS. Patients undergoing immediate, delayed or delayed-immediate reconstruction with either a deep inferior epigastric perforator (DIEP) or transverse upper gracilis (TUG) flap were included in the study. Delayed immediate reconstruction was defined as a microsurgical breast reconstruction procedure when the patient previously underwent mastectomy and temporary expander placement to preserve the breast skin. For bilateral procedures, immediate and delayed reconstructions were defined as one side being an immediate microsurgical reconstruction after mastectomy and one side as being a delayed microsurgical reconstruction when the patient previously underwent mastectomy. All procedures were performed by the ten consultant plastic surgeons at a single centre. There were no exclusion criteria. One hundred and thirty-eight patients were
identified from hospital coding records within that period as having undergone a microsurgical breast reconstruction procedure and were included in the study. All case notes were available for review and statistical analysis.

Demographic data collected from patients’ clinical records included age, body mass index (BMI), breast cancer laterality, whether the patient received chemotherapy and/or radiotherapy, past medical and surgical history, current medications and smoking status. Operative data included the type of flap performed, antibiotic choice at induction, tranexamic acid use, average body temperature, volume of fluid administered and analgesia details. Postoperative data included the total amount of daily analgesia, haemoglobin change, time to catheter removal, time to independent mobilisation, daily output and timing of surgical drain removal as well as LOS. Complications were defined and recorded according to the classification of surgical complications, minor complication defined as grade 1 (any deviation from the normal post-operative course without the need for pharmacological treatment or surgical, endoscopic and radiological interventions) and major defined as grade 2 (requiring pharmacological treatment with drugs other than those allowed in grade 1 complications) or 3 (requiring surgical, endoscopic or radiological intervention).20

Outcome measures

The primary outcome measures were hospital LOS, which was defined as the number of days from the operation to discharge and complication rates. Secondary outcome measures included unplanned readmission and return to theatre. Other endpoints measured were time to independent mobilisation, time to catheter removal, time to removal of patient-controlled analgesia (PCA) and time to drain removal, all of which were recorded in days from the operation and total opioid use which was calculated by converting parenteral and oral opioid doses into intravenous morphine equivalent.

Enhanced recovery after surgery pathway

The ERAS pathway was developed by a multidisciplinary team of plastic surgeons, anaesthetists, specialist nurses and pharmacists. Our ERAS pathway consisted of three phases to optimise patient care: preoperatively, intraoperatively and post-operatively.

A preoperative optimisation phase included counselling and education about the operation and post-operative recovery period, a smoking cessation recommendation at least six weeks prior to surgery and optimisation of nutrition and BMI of ≤35, aiming to reduce post-operative complication risk.21 All non-diabetic patients received a high-carbohydrate clear fluid drink the evening before surgery and two hours before induction to minimise the catabolic effects of surgery and the post-operative recovery period.22

Intraoperatively, patients received teicoplanin at induction or alternative in case of known allergy.23 In addition to low molecular weight heparin and post-operative TED stockings, the ERAS group received intraoperative Flowtron boots (ArjoHuntleigh AB, Eslov, Sweden) as mechanical deep vein thrombosis prophylaxis.24 The majority of patients received 1000 mg of tranexamic acid with the aim to limit blood loss although one consultant plastic surgeon opted out of this part of the ERAS pathway.25 The volume of intravenous fluids and intraoperative opioids was at the discretion of the anaesthetist, but the objective was to maintain euvoilaemia as fluid overload has been shown to increase surgical morbidity in microsurgical procedures.26 Normothermia was encouraged pre-operatively with the use of foil blankets and a forced air warming device (Bair Hugger) was used intraoperatively and post-operatively.27 Patients received intraoperative passive movement therapy to limit non-surgical site pain post-operatively.28 At the end of the procedure, they received a rectus sheath block to the donor site using 40 ml of 0.5% chirocaine.29

Post-operatively, patients had a PCA pump and standard analgesia using paracetamol, non-steroidal anti-inflammatory drugs and oral opioids for breakthrough pain once the PCA pump was removed, preferably on the first post-operative day (POD 1). In addition, they all received three consecutive doses of 600 mg of Gabapentin (one at induction and two post-operatively), which has been shown to reduce the need for opioid analgesia.30 Solid diet was resumed on the morning of the POD 1 in the absence of complications. Patients were placed in an abdominal binder and support bra on POD
1. Independent mobilisation was also encouraged on POD 1, and the urinary catheter was removed if appropriate. Surgical drains were kept at the surgeon’s discretion, usually removed once the daily output was ≤30–50 ml. In the absence of complications, patients were discharged when independently mobile, pain controlled with oral analgesia, a solid diet resumed and all surgical drains removed.

Statistical Analysis

Continuous variables are presented as either means (±standard deviations) or medians (25, 75 percentiles), and categorical variables are presented as numbers (percentages). Comparisons between groups were done using the independent t-test or Mann–Whitney U test for continuous variables and the χ² or Fishers exact tests for proportions, as indicated. Logistic regression was used to assess how baseline characteristics, operation type and the ERAS pathway affected complication rates. Factors affecting baseline to event data were analysed using survival analyses due to the positive skew of the time-dependent variables. Cox proportional-hazards regression models using the Enter method were used to assess the relationships with baseline and surgical variables and the presence of complications. Categorical factors affecting LOS were displayed graphically using Kaplan–Meier survival curves and were compared using the log-rank test. Odds ratios (OR) and hazard ratios (HR) are reported with 95% confidence intervals. A two-sided p value of <0.05 was considered statistically significant. All analyses were undertaken using IBM® SPSS® Statistics Version 25 (IBM Corporation).

Results

Patient demographics

One hundred and thirty-eight patients underwent breast microsurgical reconstruction over the eight-month period (January 2015–August 2015) and were included in the study. Sixty-six patients were treated under the ERAS pathway and 72 were treated under the TRAS pathway. Baseline demographics are illustrated in Table 1. Both groups were comparable in age (p = 0.57), BMI (p = 0.57) and all other co-morbidities (see Table 1).

Flap data

One hundred and nine patients underwent unilateral reconstruction and 29 patients had bilateral reconstructions. Details of flap reconstruction data are given in Table 2. There was no significant difference in the number of immediate, delayed and delayed-immediate procedures or the type of procedure (DIEP or TUG flap) in the ERAS cohort versus the TRAS cohort in patients who underwent

| Table 1 | Baseline demographic data comparing the ERAS and TRAS patient groups. |
|--------|---------------------------------------------------------------------|
|        | ERAS (n=66) | TRAS (n=72) | p value |
| Age (years) | 53.5±9.4 | 52.6±8.2 | 0.57 |
| BMI (kg/m2) | 27.3±3.6 | 27.6±3.4 | 0.57 |
| Smoking history | 56 (85) | 66 (92) | 0.24 |
| Never | 1 (2) | 2 (3) | 0.10 |
| Current | 9 (14) | 4 (6) | 0.07 |
| Prior chest irradiation | 31 (47) | 42 (58) | 0.18 |
| Prior chemotherapy | 33 (50) | 39 (54) | 0.62 |
| Prior hormonal therapy | 31 (47) | 44 (61) | 0.10 |
| Hypertension | 5 (8) | 6 (8) | 0.87 |
| Diabetes | 0 (0) | 1 (1) | 0.52 |
| Asthma/COPD | 1 (2) | 1 (1) | 0.73 |
| Thromboembolism | 1 (2) | 1 (1) | 0.73 |
| Ischaemic heart disease | 0 (0) | 2 (3) | 0.27 |

ERAS – enhanced recovery after surgery and TRAS – traditional recovery after surgery
Table 2
Distribution of surgical reconstruction methods between the two ERAS and TRAS patient groups.

|                      | ERAS (n=66) | TRAS (n=72) | p value |
|----------------------|-------------|-------------|---------|
| **Unilateral flap (n=109)** |             |             |         |
| **Immediate**        |             |             |         |
| DIEP                 | 19 (29)     | 17 (23)     | 0.71    |
| TUG                  | 4 (6)       | 1 (1)       | 0.20    |
| **Delayed**          |             |             |         |
| DIEP                 | 25 (38)     | 33 (46)     | 0.64    |
| TUG                  | 0 (0)       | 3 (4)       | -       |
| **Delayed immediate**|             |             |         |
| DIEP                 | 3 (5)       | 1 (1)       | 0.36    |
| TUG                  | 2 (3)       | 1 (1)       | 0.61    |
| **Bilateral flaps (n=29)** |           |             |         |
| **Immediate**        |             |             |         |
| DIEP                 | 7 (11)      | 6 (8)       | 0.78    |
| TUG                  | 0 (0)       | 0 (0)       | -       |
| **Delayed**          |             |             |         |
| DIEP                 | 2 (3)       | 6 (8)       | 0.28    |
| TUG                  | 1 (2)       | 0 (0)       | -       |
| **Immediate and delayed** |         |             |         |
| DIEP                 | 3 (5)       | 3 (4)       | 1.00    |
| TUG                  | 0 (0)       | 1 (1)       | -       |

ERAS – enhanced recovery after surgery, TRAS – traditional recovery after surgery, DIEP – deep inferior epigastric perforator and TUG – transverse upper gracilis

Table 3
Post-operative outcomes between the two ERAS and TRAS patient groups.

|                      | ERAS (n=66) | TRAS (n=72) | p value |
|----------------------|-------------|-------------|---------|
| LOS (days)           | 4.0 (3.0, 4.25) | 4.0 (3.0, 5.0) | 0.48    |
| Time to catheter removal (days) | 1.0 (1.0, 2.0) | 2.0 (1.0, 2.0) | <0.01   |
| Time to mobilisation (days)      | 2.0 (1.0, 2.0) | 2.0 (2.0, 2.75) | <0.01   |
| All drains removed (days)        | 3.0 (2.0, 4.0) | 3.0 (2.0, 4.0) | 0.49    |
| Hb reduction (g/dL)              | 22.2±8.6    | 26.2±10.9   | 0.02    |
| Time to PCA down (days)          | 1.0 (1.0, 2.0) | 2.0 (1.0, 2.0) | <0.01   |
| Opioids (iv morphine equivalent, mg) |             |             |         |
| POD 0                          | 22.0 (16.8, 29.3) | 24.0 (18.4, 30.1) | 0.29    |
| POD 1                          | 3.3 (0.9, 9.1)  | 7.8 (3.0, 12.0) | <0.01   |
| POD 2                          | 0.3 (0.0, 4.0)  | 2.0 (0.0, 4.5) | 0.15    |
| POD 3                          | 0.0 (0.0, 1.0)  | 0.0 (0.0, 1.0) | 0.54    |
| Total                          | 27.0 (19.9, 41.1) | 38.0 (25.5, 49.5) | 0.01    |

ERAS – enhanced recovery after surgery, TRAS – traditional recovery after surgery, LOS – length of stay, PCA – patient controlled analgesia and POD – postoperative day

unilateral reconstruction. Similarly, in the bilateral group, there was no significant difference in the type of procedure and the number of immediate versus delayed reconstructions in each cohort.

Length of stay and post-operative outcomes

Post-operative outcome data are presented in Table 3. We found no significant difference in hospital LOS in the ERAS (4.0 (3.0, 4.25) days) versus the TRAS groups (4.3 (3.0, 5.0) days), p=0.48. There was a trend towards a significant reduction in return to theatre in the ERAS group (7 (11%) versus 15 (21%), p=0.10), and there was a non-significant reduction in the readmission rate in the ERAS group (4 (6%) versus 8 (11%), p=0.29).

There were significant reductions in the time to catheter removal (HR 0.7 (0.5-0.9, p=0.02), independent mobilisation (HR 0.7 (0.5-1.0, p=0.03) and time to removal of the PCA (HR 0.7 (0.5-1.0, p=0.07), all in favour of the ERAS group. Time to drain removal was unchanged between the two groups (HR 0.9 (0.6-1.3, p=0.55). Multivariable analysis showed that of the remaining three factors,
only the time taken to remove the drains remained linked to LOS (HR 0.64 (0.53-0.76), p<0.001). A binned scatterplot illustrating this close relationship is shown in Figure 1.

The post-operative drop in haemoglobin was significantly greater in the TRAS group (22.2 ±8.6 and 26.2±10.9 g/dL, p=0.02 in ERAS and TRAS, respectively). This may have related to the trend towards a statistically significant reduction in the volume of intraoperative fluids administered in the ERAS versus TRAS groups (2370 versus 2690 ml, p=0.08) and the trend towards higher usage of tranexamic acid at anaesthetic induction in the TRAS versus ERAS groups (37 (56%) versus 29 (40%), p=0.08). There were no post-operative blood transfusions in any patient. Recovery (37±0.4°C) and intraoperative (36±0.5°C) temperatures were identical in both groups.

There was a significant reduction in the total usage of opioid analgesia in the ERAS group (27.0 (19.9, 41.1) versus 38.0 (25.5, 49.5) mg IV morphine equivalent, p=0.01). This was driven by reduced usage on POD 1 and was corroborated by a significantly reduced amount of time to removal of the PCA pump (1.0 (1.0, 2.0) versus 2.0 (1.0, 2.0) days, p<0.01, see Table 3).

Overall, only obesity (BMI≥30) from the variables in Tables 1 and 2 affected LOS (HR 1.7 (1.2-2.5, p=0.007). Surgical pathway did not reduce LOS (HR 0.9 (0.7-1.3), p=0.62). Overall, the presence of a complication significantly prolonged LOS (HR 1.5 (1.2-2.2), p=0.02), see Figure 2. Minor but not major complications were related to the presence of obesity (13/41 (32%) versus 14/83 (17%) p=0.02), see Figure 3. After multivariable analysis, both obesity (HR 1.7 (1.1-2.5, p<0.01) and the presence of any complication (HR 1.5 (1.1-2.2), p=0.02) remained predictors of prolonged LOS.

**Complication rates**

There was a significant reduction of the total number of complications in the ERAS group (17 (26%) versus 34 (47%), p=0.01). When Grade I complications were excluded, there remained a statistically significant reduction in major complications within the ERAS versus TRAS groups (7 (11%) versus 17 (24%), p=0.04). The difference appears to have been driven by a reduction in wound infections, seromas and haematomas (see Table 4).
Figure 2. Kaplan–Meier curve showing the highly significant relationship between the occurrence of complications and patient length of stay in the overall study population.

Figure 3. Kaplan–Meier curve showing the relationship between the presence of obesity and patient length of stay in the overall study population.
In the overall study population, there was a highly significant correlation between the presence of complications and obesity on LOS, as described above. None of the baseline variables in Table 1 or type of operation in Table 2 significantly predicted overall complication risk. Only the ERAS pathway (OR 0.4 (0.2-0.8), p=0.01) was a predictor of lower overall complication rate. Furthermore, the ERAS pathway was also a predictor of lower major complication rates (OR 0.4 (0.1-1.0), p=0.049).

Discussion

ERAS pathways have been established in many surgical disciplines as the gold standard of perioperative care because of improved surgical outcomes by reducing morbidity and LOS as well as standardising care.5-13 Only a few reports have been published using enhanced recovery following microsurgical breast reconstruction.14-18 Batdorf et al. were the first to introduce a structured enhanced recovery programme after breast microsurgical reconstruction.14 Although their ERAS and TRAS group were quite heterogenous with the ERAS cohort having a lower BMI, less chronic pain and a higher rate of DIEP flap reconstruction, their results showed that ERAS pathways were safe and effective in breast microsurgical reconstruction. They demonstrated a reduction of LOS from 5.5 to 3.9 days as well as decreased opioid use without an increase in complication rate. Authors from the same unit subsequently expanded the patient cohort by 2 years and included a cost analysis that showed a decrease in overall mean costs in the ERAS group.15 Bonde et al. found similar results following implementation of their fast-track surgery pathway with a reduction of mean LOS from 7.4 to 6.2 days with a similar number of complications in both groups.15 They achieved a further reduction in LOS from 6.2 to 3.1 days after refining their fast-track protocol by identifying factors that kept patients in hospital.18 Afonso et al. also showed a reduced mean LOS from 5 to 4 days as well as lower opioid requirement in their enhanced recovery cohort of 42 patients compared with controls. Temple Oberle et al. recently published international guidelines from the ERAS society for perioperative care in breast reconstruction consisting of 18 recommendations.11 A subsequent study by the same group using those guidelines showed a reduced LOS from 6.6 to 4.8 days as well as an 88% reduction of parenteral opioids in the 72 patients included in their enhanced recovery group compared with their traditional recovery group.17

To date, our study is the first to report a reduction in the number of complications in patients undergoing breast microsurgical reconstruction with an ERAS perioperative care model. This was the

Table 4
Minor and major complication rates between the ERAS and TRAS patient groups.

| All complications | ERAS (n=66) | TRAS (n=72) | p value |
|-------------------|------------|------------|---------|
| **Grade 1**       |            |            |         |
| Cellulitis        | 7 (11)     | 10 (14)    |         |
| Seroma            | 0 (0)      | 4 (6)      |         |
| Delayed wound healing | 2 (3)    | 2 (3)      |         |
| Fat necrosis      | 0 (0)      | 1 (1)      |         |
| Thrombocytopenia  | 1 (2)      | 0 (0)      |         |
| **Total minor complications** | 10 (15) | 17 (24) |         |
| **Grade ≥ 2**     |            |            |         |
| Deep vein thrombosis | 0 (0)    | 1 (1)      |         |
| Pneumonia         | 0 (0)      | 1 (1)      |         |
| Wound infection/debridement | 0 (0) | 1 (1) |         |
| Haematoma evacuation | 3 (5)   | 6 (8)      |         |
| Abscess/collection | 2 (3)     | 3 (4)      |         |
| Mastectomy skin flap necrosis | 0 (0) | 2 (3) |         |
| Anastomosis revision | 1 (2)    | 1 (1)      |         |
| Partial flap failure | 1 (2)    | 1 (1)      |         |
| Total flap failure | 0 (0)      | 1 (1)      |         |
| **Total major complications** | 7 (11) | 17 (24) | 0.04    |
| **Overall complication rate** | 17 (26) | 34 (47) | 0.01    |

ERAS – enhanced recovery after surgery and TRAS – traditional recovery after surgery
case for both major (24% in the TRAS group versus 11% in the ERAS group) and overall complication rates (47% in the TRAS group versus 24% in the ERAS group).

Major complications rates vary significantly in other published series following the introduction of an enhanced recovery pathway in breast microsurgical reconstruction, ranging from 9.5% to 22.7% in pre-enhanced recovery cohorts and from 8.3% to 33% in enhanced recovery groups.\textsuperscript{14-17} Our major complication rates were similar at 24% in the TRAS group and 11% in the ERAS group, although there was a significant decrease following the introduction of the pathway, mostly in infectious complications and haematomas. It is difficult to establish which constituents of the ERAS pathway are responsible for the lower complication rate that was achieved. A recent study by Watts et al. focused at which components of an ERAS pathway impact on the surgical stress response in colorectal surgery and found that while early feeding and mobilisation have been shown to decrease LOS, objective evidence of the impact of individual components of the ERAS pathway on the surgical stress response is limited.\textsuperscript{32}

Similar to other studies, we found a decrease in total intravenous morphine equivalent of 29%, this was most likely driven by the addition of gabapentin to the pathway, passive movement therapy and rectus sheath block intraoperatively as well as the earlier removal of the PCA pump. Preoperative warming in the ERAS group did not affect intra- and post-operative temperatures and thus may not be an effective protocol adjunct.

Although the hospital LOS was unchanged in both groups (4.0 days) in our study, even our TRAS group had an LOS equal or shorter than most published ERAS groups ranging from 3.9 to 6.2 days, demonstrating a pre-existing highly efficient discharge pathway. Only Bonde et al., to date, have managed to achieve a shorter LOS of 3.1 days, but this was on a limited number of patients with only unilateral delayed breast reconstructions.\textsuperscript{18}

A rate limiting step that influenced LOS in a significant proportion of our patients was the time taken to remove surgical drains. Drain removal was not a feature of our ERAS pathway and remained at the discretion of the operative surgeon, usually waiting for the total output to be $\leq$30-50 ml per 24 hours before removal. In their cohort, Batdorf et al. showed a reduction in LOS following introduction of an ERAS pathway as previously described; however, they mention patients’ education about drain care, suggesting that some patients were discharged home with drains in situ. In their most recent publication, Bonde et al. successfully reduced LOS by 50% in 16 consecutive patients after further improving their fast track programme\textsuperscript{18}. One of the changes they introduced was a nurse-led removal of drains on POD 2 if the output was $\leq$50 ml or on POD 3 if the output was $\leq$100 ml, without an increase in the number of complications. In another study, Miranda et al. found that there was no increase in total complications, seroma, wound dehiscence or haematoma rates following DIEP breast reconstruction between a group of patients who had their drains removed on POD 3 regardless of the output versus another group in which drains were removed after POD 3 depending on drainage volume per 24 hours.\textsuperscript{33} It follows that incorporating a protocol regarding accelerated drain removal will be an important addition to our ERAS care pathway to reduce LOS to less than 4 days without compromising surgical outcomes.

Finally, irrespective of the recovery pathway, we found a strong correlation between obesity, complications and prolonged LOS, which is in keeping with other studies and further emphasises the importance of preoperative counselling and nutrition/weight optimisation.\textsuperscript{21,34,35}

Study Limitations

This was a single centre retrospective study with its inherent limitations. Whilst not randomised, consecutive patients with no baseline or operative differences were studied, in a high-volume multi-operator centre, making it reasonable to conclude that the majority of the study findings relate to the implementation of the described ERAS pathway.

Conclusion

ERAS pathways should be integrated into breast microsurgical reconstruction. Immediate reductions in overall and major complication rates in a high-volume tertiary centre using an already
streamlined service were observed. We encourage all plastic surgery centres to adopt the use of an ERAS pathway to reduce surgical morbidities and improve patient care. Further work should be ongoing to continually establish the optimisation of patient outcomes using ERAS pathways in the setting of breast microsurgical reconstruction.

Conflict of interest statement

None.

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