

Retrospective audit on time to surgery delays following the completion of neoadjuvant chemotherapy in breast cancer patients

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Abstract. The ideal time to surgery interval in breast cancer patients following neoadjuvant chemotherapy according to published literature is as low as 21 days, 40 days and up to 8 weeks. The authors' hospital multidisciplinary team (MDT) accepted 28 days as a reasonable time interval to allow recovery from the side-effects of neoadjuvant chemotherapy. The present retrospective clinical audit presents a review of all breast cancer cases that received neoadjuvant chemotherapy and examined the conformity to the set audit standards. The primary aim of the present audit was to investigate the time interval from the conclusion of neoadjuvant chemotherapy to surgery in breast cancer patients, and to determine the causes of potential delays and identifying means to improve the outcomes of the current process. The secondary objectives were to investigate the timing of tumour coil insertion, the timing of surgical planning multidisciplinary team meeting, the time to addition to the surgical waiting list and whether these patients had adequate tumour monitoring for effective surgical planning. A total of 59 breast cancer patients who had received neoadjuvant chemotherapy from November 1, 2011 to October 31, 2016 were identified. In total, one primary audit standard and six secondary audit standards were derived from the MDT consensus agreement and reasons for non-conformity to these standards were audited. The primary standard was described as 'surgery should be performed within 28 days of completion of last cycle of neoadjuvant chemotherapy'. The results revealed that conformity to this standard was 14%. The conformity of secondary standards was also poor, ranging from 20 to 98%. The results of the present audit were not very encouraging. Recommendations were drawn with a plan for

a re-audit following the implementation of changes agreed upon by the multidisciplinary team and a plan of action was prepared. It was concluded that achieving a time to surgery interval of <28 days following the completion of neoadjuvant chemotherapy is an achievable challenging task and only possible with an efficient multidisciplinary team work.

Introduction

The optimal time interval between the end of neoadjuvant chemotherapy and definitive surgery is unclear. Some published large randomized clinical trials have revealed no significant differences in disease-free and overall survival between patients receiving chemotherapy in the adjuvant and the neoadjuvant settings (1-4).

To date, to the best of our knowledge, no large randomized clinical trials on neoadjuvant systemic therapy have addressed the issue of delays in the time to surgery following the completion of neoadjuvant chemotherapy and its effect on survival outcomes. To the best of our knowledge, there are three retrospective studies that have investigated the effects of the time to surgery following neoadjuvant chemotherapy on survival outcomes (5-7). A prolonged time to surgery interval may theoretically increase the risk of recurrence by allowing tumour neo-angiogenesis and tumour growth.

The breast multidisciplinary team at Medway Hospital (Gillingham, UK) agreed that upon an ideal time to surgery interval of ≤ 28 days, which would allow a reasonable amount of time for recovery from the side-effects of neoadjuvant chemotherapy without compromising the survival outcomes.

The present retrospective clinical audit presents a review of all breast cancer cases that received neoadjuvant chemotherapy followed by surgery and examines the conformity to the set audit standards.

Patients and methods

The present retrospective clinical audit presents a review of all female breast cancer patients following neoadjuvant chemotherapy followed by surgery to establish conformity to the set audit standards. The exclusion criteria were male breast cancer patients and metastatic breast cancer patients.

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A total of 59 breast cancer cases that received neoadjuvant chemotherapy that satisfied the inclusion and exclusion criteria at Medway Hospital between November 1, 2011 and October 31, 2016 were included in the audit. The details of the patients included in the present audit are listed in Table I.

Audit standards. In total, one primary audit standard and six secondary audit standards were derived from the Medway hospital Multidisciplinary Team (MDT) consensus agreement and the reasons for non-conformity to these standards were audited.

Primary audit standard. All patients should have a time to surgery within 28 days of completion of the last cycle of neoadjuvant chemotherapy.

Secondary audit standards. i) All cases should undergo MDT discussion prior to the completion of the last cycle of neoadjuvant chemotherapy; ii) all cases should be added to the surgical waiting list prior to the completion of the last cycle of neoadjuvant chemotherapy; iii) all cases should have surgery <4 weeks following the addition to the waiting list; iv) all cases should have tumour coil insertion prior to the commencement of the first cycle of neoadjuvant chemotherapy; v) all cases should have mid-chemotherapy imaging to assess the tumour response to neoadjuvant chemotherapy; vi) all cases should have post-neoadjuvant chemotherapy imaging to aid in surgical planning.

The time to surgery following the completion of neoadjuvant chemotherapy, the timing of surgical planning multidisciplinary team meeting, the time to addition to the surgical waiting list, tumour coil insertion timing, percentage of cases who had mid-chemotherapy imaging and post-neoadjuvant chemotherapy imaging were audited. The percentage of conformity to the aforementioned standards was calculated and factors contributing to non-conformity were investigated. Data were extracted by the reviewing of existing medical records, clinical letters, radiology reports, laboratory reports and the trust oncology database. All data and records generated during the study were kept secure and confidential in accordance with trust policies on information governance and data protection.

Results

Primary standard. All cases should have surgery ≤ 28 days following the completion of the last cycle of neoadjuvant chemotherapy. In the present audit, only 14% of patients conformed to this standard. The details of non-conformed cases (86%) are illustrated in Fig. 1.

The causes for delays in time to surgery were adverse events (16%), surgical planning delays in bilateral mastectomy patients (12%), issues related to wire localization in wide local excision cases (37%) and unknown causes (35%). The adverse events noted were side-effects from chemotherapy and persistent symptoms requiring additional imaging to rule out metastasis. In total, three quarters of the non-conformed cases with adverse events (75%) had surgery at ≥ 6 weeks following the completion of the last cycle of neoadjuvant chemotherapy. Furthermore, 37% of these cases waited >4 weeks on the waiting list, resulting in further delays. The causes for surgical delays in the non-conformed cases are illustrated in Fig. 2.

Table I. Details of age distribution, type of breast cancer, receptor positivity and type of surgery performed in the patients included in the audit.

Parameter	No. of patients
Age groups	
31 to 50 years	33
51 to 70 years	24
71 to 80 years	2
Tumour type	
Invasive ductal carcinoma	53
Invasive lobular carcinoma	5
Basal type	1
Tumour grade	
Grade 1	0
Grade 2	19
Grade 3	40
Receptor status (ER, PR, HER2)	
Triple-negative (ER ⁻ , PR ⁻ and HER2 ⁻)	22
ER ⁺ , PR ⁺ and HER2 ⁻	10
HER2-positive only (ER ⁻ , PR ⁻ and HER2 ⁺)	12
ER ⁺ , PR ⁻ and HER2 ⁺	3
ER-positive only (ER ⁺ , PR ⁻ and HER2 ⁻)	8
Triple-positive (ER ⁺ , PR ⁺ and HER2 ⁺)	4
Type of surgery performed	
Mastectomy	22
Wide local excision with no wire localisation	14
Wide local excision with wire localisation	23

ER, estrogen receptor; PR, progesterone receptor; HER2, human epidermal growth factor receptor 2.

Time to surgery delays in bilateral mastectomy patients were secondary to the need for multiple patient consultations, such as genetic counselling, genetic testing and to facilitate the patient's informed choice of reconstruction.

The cases with wire localised wide local excision had surgery >6 weeks following the completion of their last cycle of neoadjuvant chemotherapy in 53% of the cases and waited >4 weeks after being added to the waiting list in 79% of cases, resulting in further delays.

For cases undergoing wire guided wide local excision, both a surgical theatre slot and a wire localisation radiology appointment on the day of surgery is a necessity. This is an important contributing factor for non-conformity in the present cohort of patients. Wire localization procedures are only performed by radiologists at Medway Hospital. This issue may have been overcome by dedicated wire localization slots for these high-risk patients. Some hospitals have trained radiographers taking over these lists, offloading already strained consultant-led radiology services.

A total of 35% of the non-conformity cases were due to unknown causes. Over-booked clinics and long surgical waiting lists and communication delays between oncologists and surgeons may have contributed to the delays in these cases.

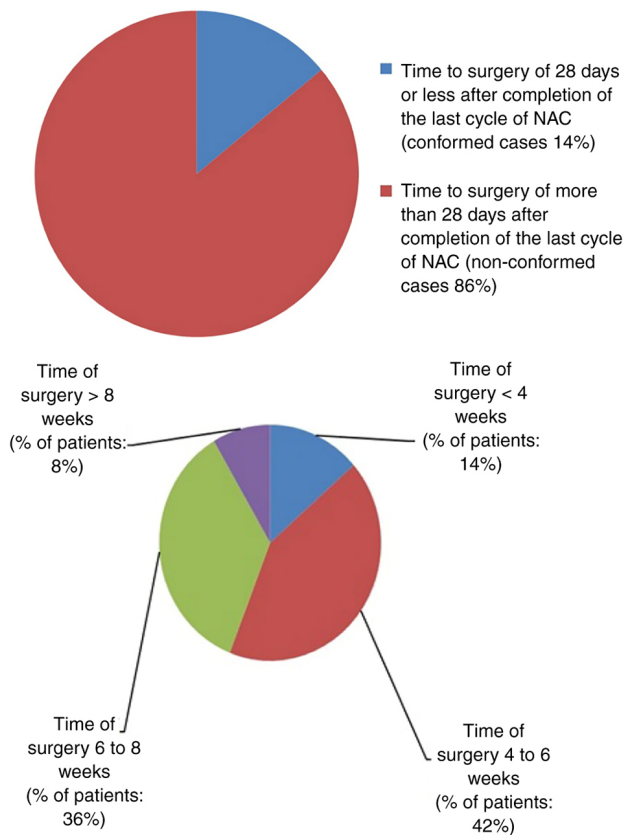


Figure 1. Time to surgery following the completion of the last cycle of NAC. NAC, neoadjuvant chemotherapy.

Achieving the target time to surgery interval of ≤ 28 days is inter-dependent on other factors, including an efficient multidisciplinary approach and effective waiting list management. Further studies with larger sample sizes are required to provide insight into the ideal time to surgery following the completion of neoadjuvant chemotherapy and its effect on survival outcomes.

Secondary audit standard 1. All cases should be discussed in surgical planning multidisciplinary meetings prior to the completion of the last cycle of neoadjuvant chemotherapy. Multidisciplinary meetings for surgical planning should be ideally timed close to the completion of the last cycle of chemotherapy. This will facilitate the addition of these cases promptly to the waiting list and reduce time to surgery delays. Mid-treatment multidisciplinary meetings in non-responsive cases provides an opportunity to determine whether surgery is an option. These discussions were usually planned by the oncologists to expedite surgery in these unresponsive cases. The policy is to discuss all neoadjuvant chemotherapy cases in multidisciplinary meetings for surgical planning prior to the completion of the last dose of chemotherapy and mid-treatment multidisciplinary meetings are held for unresponsive cases.

In the present audit, only 25% of the patients conformed to this standard. Out of the 75% non-conforming cases, no multidisciplinary meetings were held for 7% of the cases. These cases were added to the waiting list directly from the clinic. No apparent reason was found in these cases

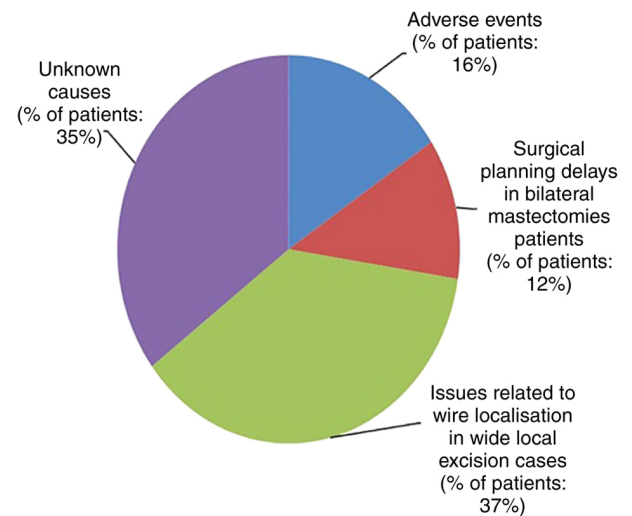


Figure 2. Causes for time to surgery delays in non-conformity cases.

The details of non-conformed cases (75%) are illustrated in Fig. 3

Secondary standard 2. All cases should be added to the waiting list prior to the completion of last cycle of neoadjuvant chemotherapy. Adding these high-risk patients to the waiting list soon after their surgical planning multidisciplinary team meeting and effective waiting list management will reduce the delays in time to surgery. The unit policy is to add all neoadjuvant chemotherapy cases to the waiting list prior to completion of the last cycle for effective patient flow management. This is done in the next available breast clinic by breast surgeons.

In the present audit, only 20% of patients conformed to this standard. The details of non-conformed cases (80%) are illustrated in Fig. 4.

Secondary standard 3. All cases should have surgery <4 weeks after being added to the waiting list. The trust policy is to perform surgery within 4 weeks after being added to the waiting list. Effective waiting list management is a key element in reducing time to surgery delays in this high-risk cohort of patients. This is mainly performed by consultant secretaries and managerial staff. Good communication is crucial for optimal outcomes. Maintaining pooled surgical consultant waiting list and dedicated wire localisation slots for neoadjuvant chemotherapy cases may reduce time to surgery delays.

In the present audit, only 66% of patients conformed to this standard; 34% of non-conformity cases were due to oversubscribed surgical waiting lists and issues related to overbooked wire localisation lists. Some of these non-conformity cases also had delays being added to the waiting list, which further contributed to the delays in time to surgery with on obvious reason. These results are illustrated in Fig. 5.

The results of the present audit revealed very poor conformity with the audit standards. Multidisciplinary coordination appears to be the means with which to improve the conformity

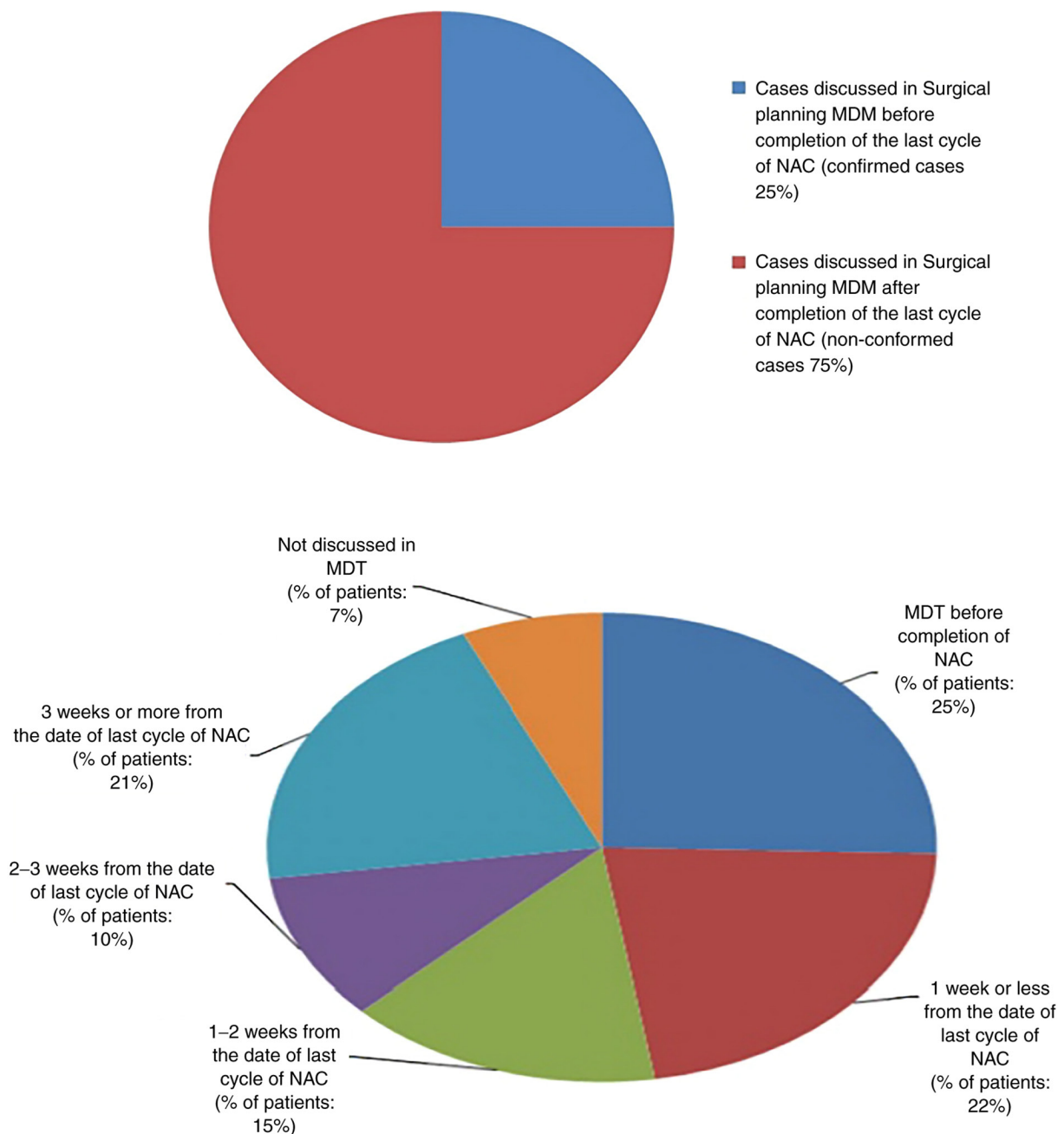


Figure 3. Time to surgical planning MDM following the completion of the last cycle of NAC. NAC, neoadjuvant chemotherapy; MDM, multidisciplinary meeting.

to the standards for better patient outcomes of these high-risk patients. These results were discussed in the Medway hospital NHS trust audit and clinical governance meeting and MDT recommendations were drawn to achieve the target of time to surgery of ≤ 28 days.

Secondary audit standard 4. All cases should have tumour coil insertion before the commencement of the first cycle of NAC. Conformity to this standard was 36%.

Secondary audit standard 5. All cases should have mid-chemotherapy imaging to assess the tumour response. Conformity to this standard was 98%.

Secondary audit standard 6. All cases should have post-NAC imaging to aid surgical planning. Conformity to this standard was 30%.

Discussion

The timing of surgery following neoadjuvant chemotherapy in breast cancer patients is paramount. There is published evidence in the form of retrospective studies which investigated the impact of time to surgery after neoadjuvant chemotherapy on survival outcomes.

Sanford *et al* (5) suggested that those patients with neoadjuvant chemotherapy to surgery intervals of up to 8 weeks

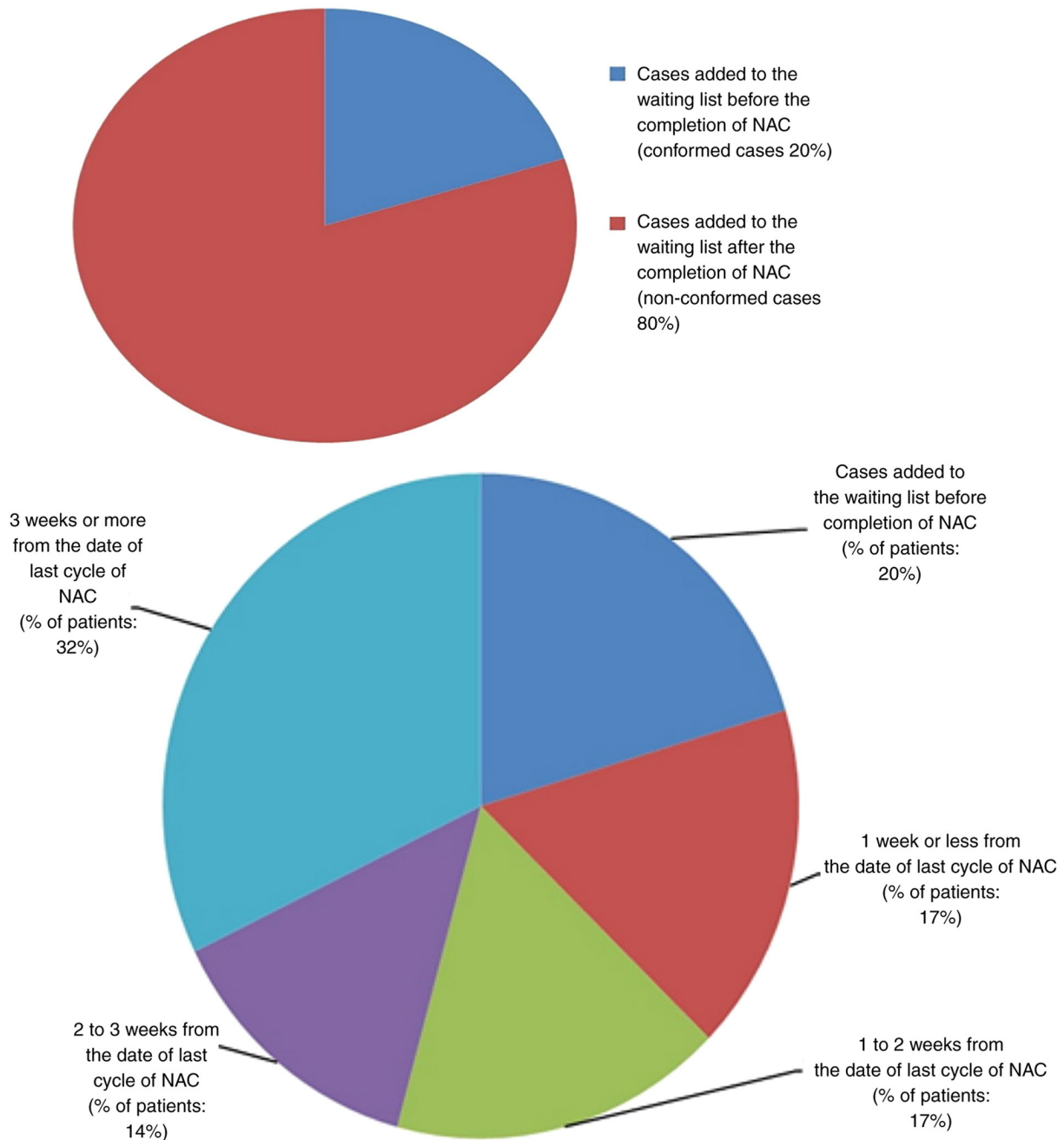


Figure 4. Time to date added to the waiting list following the completion of NAC. NAC, neoadjuvant chemotherapy.

had equivalent overall survival, recurrence-free survival and loco regional recurrence-free survival rates. Omarini *et al* (6) concluded that breast cancer patients who underwent surgery within 21 days experienced maximal benefit from previous treatment and this advantage is consistent and maintained over time.

Prolonged time to surgery intervals may theoretically increase the risk of recurrence by allowing tumour neo-angiogenesis and tumour growth. Some studies have suggested that significant reductions in Ki-67 expression following neoadjuvant chemotherapy have been shown to be associated with decreased recurrence rates. For example, Gabordi *et al* reported that patients who underwent surgery >40 days following neoadjuvant chemotherapy had lesser reductions in Ki-67 levels, potentially indicating tumour regrowth and predicting a worse oncologic outcome (7).

Our breast multidisciplinary team at Medway hospital agreed that the ideal time to surgery interval was ≤ 28 days which will allow a reasonable time for recovery from the side-effects of chemotherapy without compromising the survival outcomes.

Hence, the primary standard of this audit was derived as 'surgery should be performed within 28 days of completion of last cycle of neoadjuvant chemotherapy'. Only 14% of cases conformed with this standard. The secondary standards data analysis suggested that these surgical delays were mainly due to chemotherapy side-effects, persistent symptoms requiring scans, surgical planning MDM delays, clinic appointments delays, and long waiting lists. Unnecessary delays can affect the survival outcomes of those high-risk patients. Following the presentation of the results of this audit at the Medway

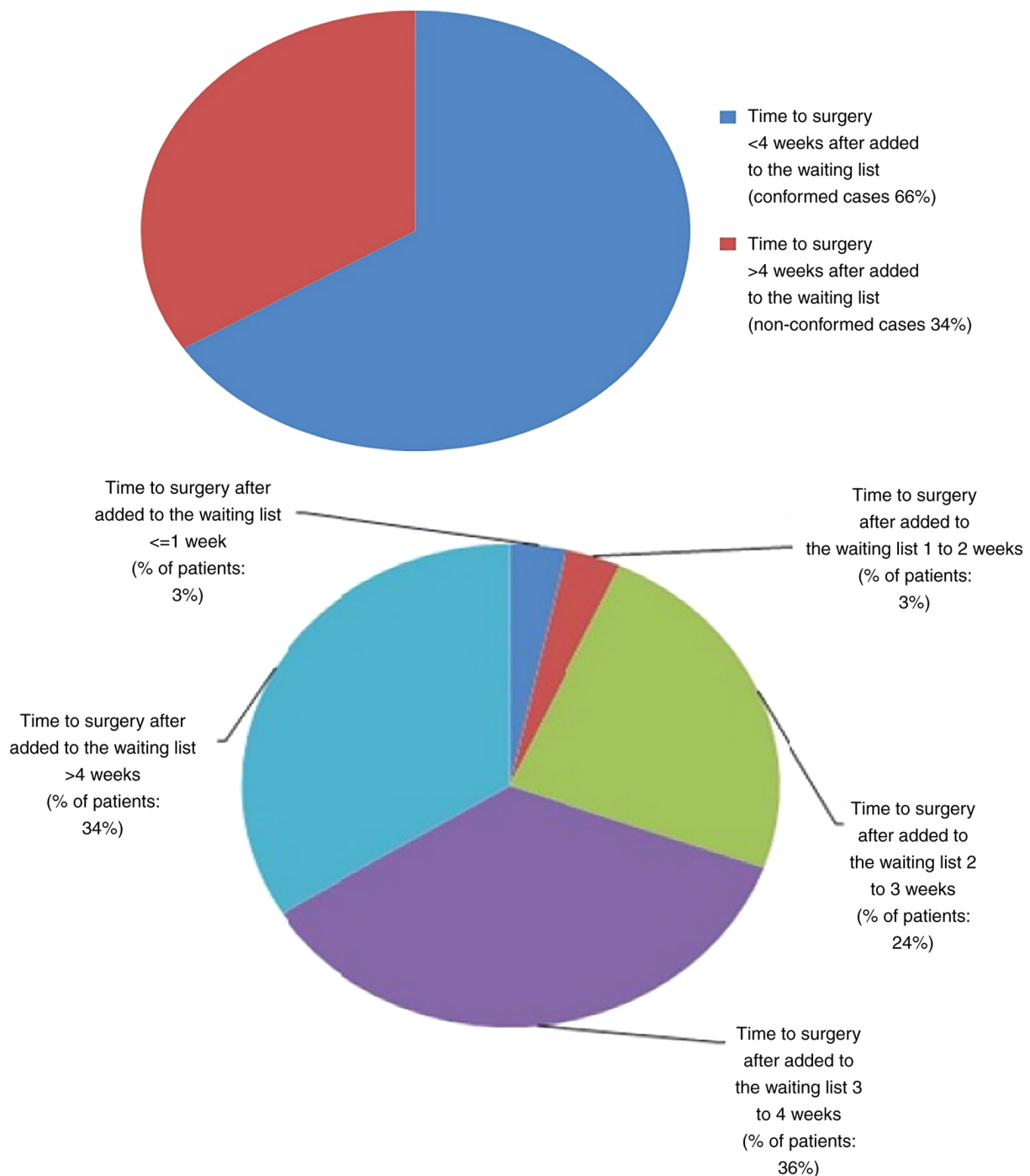


Figure 5. Time from date added to the waiting list to surgery.

hospital NHS trust audit and clinical governance meeting, recommendations were made by the breast multidisciplinary team and an action plan was formulated.

Recommendations and Action plan. Medical oncologists need to ensure that coil insertion is performed prior to the commencement of chemotherapy, mid-chemotherapy imaging is performed to assess the tumour response and imaging is performed following the penultimate cycle of neoadjuvant chemotherapy; multidisciplinary meetings should also be booked following the treatment scan results in order to aid surgical planning in collaboration with radiologists and breast surgeons.

Breast surgeons need to ensure the addition to the waiting list following surgical planning multidisciplinary meetings. Pooled waiting lists for all consultants may be helpful for reducing the surgical waiting time to <28 days. Radiologists also need to ensure dedicated slots on wire localization lists to reduce further delays. The results of the present audit were discouraging. Recommendations were drawn with the aim of re-auditing following the implementation of the changes agreed upon by the MDT.

In conclusion, achieving a time to surgery of <28 days following the completion of neoadjuvant chemotherapy is a complex and challenging process, which is inter-dependent on

a variety of factors. An effective multidisciplinary approach with efficient patient flow management and prioritising high-risk patients is necessary to achieve this target. The team efforts of oncologists, radiologists and breast surgeons will help to overcome the challenges involved and to provide improved patient care.

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Availability of data and materials

The availability of datasets used and/or analysed during the current study are available only from the corresponding author on reasonable request subjected to prior approval by the Medway Hospital Ethics and clinical Governance Committee.

Authors' contributions

BSP was involved in the conception and design of the audit, in data collection and analysis, and in the writing, revising and reviewing of manuscript. DH, AK, CA and IA were involved in the conception and design of the audit, and in the revising and reviewing of the manuscript. BSP and IA confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present clinical audit was registered with the Medway Hospitals Audit and Clinical Effectiveness Committee.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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