Investigating Barriers to Timely Surgery for Breast Cancer in Rwanda

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Scholarly Report submitted in partial fulfilment of the MD Degree at Harvard Medical School

Date: 25 February 2019

Student Name: Lauren E. Schleimer

Scholarly Report Title: Investigating Barriers to Timely Surgery for Breast Cancer in Rwanda

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Abstract

**TITLE:** Investigating Barriers to Timely Surgery for Breast Cancer in Rwanda

**Background:** Timely and high-quality breast surgery must be a key element of emerging breast cancer control efforts in sub-Saharan Africa. We investigated delays in pre-operative care and the impact of on-site versus off-site surgery on time to surgery for breast cancer patients at Butaro Cancer Center of Excellence (BCCOE) in Rwanda.

**Methods:** We used a standardized data abstraction form to collect demographic data, clinical characteristics, treatments received and disease status as of November 2017 for all patients diagnosed with breast cancer at BCCOE in 2014-2015.

**Results:** During 2014-2015, 89 patients were diagnosed with stage I-III breast cancer and treated with curative intent. Of those, 68 (76.4%) underwent curative breast surgery, 12 (13.5%) were lost to follow-up, 7 (7.8%) progressed, and 2 (2.2%) declined recommended surgery. Only 32% of patients who underwent surgery had surgery within 60 days from diagnosis or last neoadjuvant chemotherapy (NAC). Median time to surgery was 122 days from biopsy if no neoadjuvant treatments were given, and 51 days from last cycle of NAC. Patients who received no neoadjuvant treatment experienced longer median time to surgery at BCCOE (180 days) than at a referral hospital in Kigali (93 days, p=0.04). Most patients (60%) experienced a disruption in pre-operative care, frequently at the point of surgical referral. Documented reasons for disruptions and delays included patient factors, clinically indicated treatment modifications, and system factors.

**Conclusions:** We observed frequent delays to surgery, disruptions in preoperative care and loss to follow-up, particularly at the point of surgical referral. There may be opportunities to improve breast cancer survival in Rwanda and other LMICs through interventions that facilitate more timely surgical care.
### Glossary of Abbreviations

<table>
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<th>Abbreviation</th>
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<tbody>
<tr>
<td>ALND</td>
<td>Axillary Lymph Node Dissection</td>
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<tr>
<td>BCCOE</td>
<td>Butaro Cancer Center of Excellence</td>
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<tr>
<td>CHUK</td>
<td>Centre Hospitalier Universitaire de Kigali</td>
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<tr>
<td>LMICs</td>
<td>Low and Middle-Income Countries</td>
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<td>MRM</td>
<td>Modified Radical Mastectomy</td>
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<tr>
<td>NAC</td>
<td>Neoadjuvant Chemotherapy</td>
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<tr>
<td>NET</td>
<td>Neoadjuvant Endocrine Therapy</td>
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<tr>
<td>PIH</td>
<td>Partners In Health</td>
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<tr>
<td>RMH</td>
<td>Rwanda Military Hospital</td>
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Description of Scholarly Project

Project Aims

Ensuring timely and high-quality breast surgery must be a key element of effective breast cancer control in sub-Saharan Africa. Previous studies at the Butaro Cancer Center of Excellence (BCCOE) in Rwanda suggested that a low rate of timely breast cancer surgery represented a key area for further investigation and quality improvement.

In this project, I aimed to investigate 1) when along the pre-operative care pathway patients experienced delays or interruptions in care prior to surgery; 2) why patients experienced delays or interruptions in care prior to surgery, if documented; 3) whether referring patients to other facilities for surgery led to increased delays to surgery; and 4) whether rates of timely surgery improved between 2012-2013 to 2014-2015.

Student Role

- **Design** – As part of an ongoing project measuring quality of breast cancer care at BCCOE, I identified delays to surgery and interruptions in pre-operative care as an area for further investigation.
- **Data Collection** – I adapted an existing database containing data on the clinical presentation, treatment and outcomes for breast cancer patients diagnosed 2012-2013 to include a new cohort of patients diagnosed 2014-2015. While adapting the database, I revised and designed new data fields to capture information about surgical referrals and delays to surgery to enable investigation of the questions identified above. I adapted the database from Microsoft Excel to Microsoft Access to enable prospective data collection, and performed the data collection for ~95% patients meeting eligibility criteria who were diagnosed in 2014-2015.
- **Data Analysis** – I performed all data cleaning and descriptive statistical analysis.
- **Writing** – I drafted and revised the manuscript, incorporating feedback from all collaborators.

Collaborator roles:

- Jean-Marie Vianney Dusengimana – assisted with identification of patient charts to enable data collection
- Catherine Kigonya and John Butonzi – clinicians who reviewed patient staging to complete missing documentation in charts
• Abirami Natarajan – performed data abstraction for ~5% of patients meeting eligibility criteria
• Aline Umwizerwa – performed outreach to patients who had been lost to follow-up
• Daniel S. O’Neil – created the database containing the 2012-2013 cohort and provided input on the adaptation and revision for the 2014-2015 cohort
• Ainhoa Costas-Chavarri, Lawrence Shulman, Nancy L. Keating, Cyprien Shyirambere, and Tharcisse Mpunga – provided input on project design, data analysis and interpretation of results
• Lydia Pace – mentored every stage of design, execution, analysis and writing of the manuscript
INTRODUCTION

Breast cancer is an increasingly important cause of morbidity and mortality in sub-Saharan Africa, where most patients present with advanced disease and outcomes are inferior to high-income countries (Vanderpuye, 2017). In recognition of this growing burden, more and more sub-Saharan African countries are developing national breast cancer control plans (Stefan, 2013).

Surgery is the primary treatment for non-metastatic breast cancer. To effectively treat breast cancer, surgical care must be delivered through an integrated, multidisciplinary approach with other treatments as indicated, including chemotherapy, hormonal therapy, targeted therapy and radiation therapy (Zujewski, 2017). Given the central role of surgery in the treatment of potentially curable disease, ensuring access to timely, high-quality breast cancer surgery must be a core component of any national breast cancer treatment strategy (Sullivan, 2015).

Several studies in low- and middle-income countries (LMICs) have described barriers to accessing breast cancer care (Gakwaya, 2008; Clegg-Lamptey, 2009; Anyanwu, 2011; Sanchez, 2015; Ross, 2017) and catastrophic expenses associated with cancer surgery (Jan, 2015). However, there are no studies that specifically examine delays to breast surgery or identify specific challenges obtaining timely, high-quality breast cancer surgery in low-income regions, including sub-Saharan Africa.

Rwanda is a low-income East African country of 12 million people (CIA World Factbook). Seventy percent of the population live in rural areas, with a heavy reliance on subsistence agriculture (FAO). In 2012, the Rwanda Ministry of Health collaborated with the non-governmental organization Partners In Health, Brigham and Women’s Hospital and Dana-Farber Cancer Institute to open Butaro Cancer Center of Excellence (BCCOE), a dedicated cancer center located within a rural public hospital and Rwanda’s first public cancer facility. Breast cancer is the most common malignancy diagnosed and treated at BCCOE. From July 2012 through April 2018, 1076 patients with breast cancer were treated at BCCOE.

We previously assessed treatment quality for patients diagnosed with breast cancer at BCCOE within the first two years of the program opening (2012-2013). We found that only 35% of patients diagnosed with potentially curable breast cancer (i.e. early-stage or locally
advanced) underwent surgery within 60 days of diagnosis or the end of neoadjuvant chemotherapy (O'Neil, 2017). These findings highlighted the need to examine when and why patients experienced delays to surgery. We were particularly interested in understanding whether referring patients to other facilities led to more delays, since centralization of cancer surgical care is a strategy implemented across high-income countries and is being advocated for cancer control in LMICs (Sullivan, 2015).

Operative capacity at BCCOE is limited by staffing, materials and infrastructure. During some periods since BCCOE’s opening in 2012, there was no surgeon on staff. Even when a surgeon is on staff, the sole general surgeon is responsible for all general surgical care at a busy district hospital. Operative capacity was routinely impacted by drug stock-outs and water outages. As a result of these limitations, many patients are referred for breast surgery at a tertiary care hospital in Rwanda’s capital city, Kigali.

We studied the timing and types of surgery received by patients diagnosed with breast cancer at BCCOE in 2014-2015. We sought to quantify delays to surgery among this cohort, characterize patients’ pathways to breast surgery, identify where on this pathway disruptions occurred, and determine whether surgery occurred on-site versus off-site and how this impacted delays. Understanding barriers to timely surgical care at Rwanda’s first public cancer referral facility can guide strategies to improve care in Rwanda and identify challenges that must be addressed to facilitate access to safe, timely and effective breast cancer surgery in the region.

**METHODS**

**Setting and treatment protocols**

Breast cancer treatment at BCCOE is provided according to standardized, nationally-approved protocols developed collaboratively by international breast cancer experts, BCCOE clinicians and the Rwanda Ministry of Health (Tapela et al, 2016). Available systemic treatments include chemotherapy (doxorubicin, cyclophosphamide and paclitaxel) and hormonal therapy (tamoxifen and letrozole). Targeted therapy for HER2 is not yet available. Before 2018, there was no radiation therapy in Rwanda and access remains limited for patients with breast cancer. Due to the advanced presentation of disease and lack of routinely available radiation therapy, Rwanda’s protocols recommend that most breast cancer patients undergo modified radical mastectomy (MRM) including axillary lymph node dissection (ALND).
At Butaro Hospital, there is one general surgeon and one operating room dedicated for general surgical care. Since surgical capacity at Butaro Hospital is limited, patients requiring cancer surgeries are frequently referred to Rwanda Military Hospital (RMH), a public referral hospital in Kigali, which has two general surgeons in addition to other surgical specialties (e.g. Orthopedics, Gynecology). Partners In Health employs a full-time nurse in Kigali who assists cancer patients referred from BCCOE to RMH with obtaining appointments and managing logistics.

**Patient population**

We used BCCOE’s electronic medical record to identify all patients who received a pathologic diagnosis of breast cancer at BCCOE between January 1, 2014 and December 31, 2015. Patients who had previously received a pathologic diagnosis of or treatment for breast cancer elsewhere were excluded.

**Data Collection**

We used a standardized data abstraction form to collect information from paper and electronic medical records at BCCOE. Data were abstracted by two co-investigators (LS and AN). The form gathered patients’ demographic and clinical characteristics, dates of all visits and types of treatments received, and disease status or loss to follow-up as of November 2017.

**Key variables**

**Main Outcomes**

**Delays to Surgery.** Limited evidence from high-income settings suggests a survival advantage if surgery is performed within 60 days of biopsy when no neoadjuvant treatment is given (Bleicher, 2016). If neoadjuvant chemotherapy (NAC) is given, the likelihood of survival may decrease if surgery occurs more than 8 weeks after the end of NAC (Sanford, 2016). No studies to our knowledge have assessed the survival impact of overall time from diagnosis to surgery among patients receiving NAC.

There is no consensus regarding the optimal duration of neoadjuvant endocrine treatment (NET) and timing of surgery when NET is given (Spring, 2016). The BCCOE protocol
stipulates neoadjuvant tamoxifen may be used as an alternative to neoadjuvant chemotherapy in select patients and recommends an initial trial of 8 weeks, continuing up to 4 months based on tumor response.

Based on the available evidence, we defined delays in surgical care as >60 days from the date of biopsy for patients who received no neoadjuvant treatment, or from the last cycle of NAC if NAC was received. Due to limited evidence, we did not define a threshold for delay to surgery for patients who received NET.

Disruptions in Care. We defined disruptions in care as events resulting in >7 day delay in receipt of scheduled NAC, >7 day delay in the date of scheduled surgery, or >30 day delay in a scheduled visit for NET (endocrine therapy is typically only provided to patients at scheduled follow-up visits). We also considered any missed visit for surgical evaluation or surgery, and changes in clinical status (other than progression) which require modifications to the treatment plan disruptions in care. Reasons for treatment disruption were collected where available; however, these were not consistently documented in the medical record.

Patient and treatment characteristics

Stage and treatment intent. Patients were staged with physical exam and either chest X-ray and abdominal ultrasound or CT Scan according to the American Joint Committee on Cancer staging manual, 7th edition (Edge, 2010). Initial treatment intent was determined by the treatment plan established at the first visit following diagnosis.

Surgery type. As operative reports were not available in the medical records reviewed, we were unable to consistently verify the type of breast surgery received and whether ALND was performed. Surgical pathology reports were reviewed to determine whether axillary lymph nodes were present in the specimen and examined.

Surgical facility. We identified whether patients received surgery at BCCOE, RMH or another facility.

Data Analysis

We characterized the sequence of treatments received by each patient and grouped patients into four trajectories of pre-operative care: no neoadjuvant treatment; NAC only; NET only; and NET then NAC in sequence. We identified when disruptions in pre-operative care
occurred, and classified documented reasons for disruptions in care as patient factors, system factors and clinical indications.

Time to surgery was analyzed using descriptive statistics to determine the proportion of patients who experienced clinically significant delays. We compared median days to surgery for patients who had surgery at BCCOE versus RMH using Wilcoxon rank-sum tests.

**Ethics Statement**

This study was approved by the Rwanda National Ethics Committee and the Partners HealthCare Institutional Review Board.

**RESULTS**

**Patients and Clinical Presentation**

Between 2014-2015, 151 patients were diagnosed with breast cancer at BCCOE. Of these, 97 patients (64%) had stage I-III disease, 45 (30%) were metastatic on presentation, and 9 (6%) had unknown stage (Table 1).

Of the 146 patients with known estrogen receptor status, 101 (69%) were estrogen receptor positive. Of the 98 patients with known HER2 status, 39 (40%) had HER2 positive disease (Table 1). Progesterone receptor status was not routinely assessed.

**Treatments Received**

Of the 151 patients diagnosed with breast cancer, 92 (61%) were initially treated with curative intent. This includes 2 patients with stage IV breast cancer and one patient with unknown stage who had incomplete staging at the time of treatment initiation. Forty-three patients (28%) were initially treated with palliative intent, including seven patients with inoperable stage III breast cancer. Sixteen patients (11%) did not return after undergoing biopsy, including 1 patient with stage III cancer (Table 1).

A majority of the 89 stage I-III patients treated with initial curative intent received some neoadjuvant treatment—either tamoxifen alone (33%), chemotherapy alone (28%), or both in sequence (10%) (Figure 1). Sixty-eight patients (76%) ultimately underwent curative breast surgery. Of the 21 patients initially eligible for curative treatment who did not undergo...
definitive breast surgery, 2 refused recommended surgery, 12 were lost to follow-up, and 7 had documented disease progression (Table 1).

Post-operatively, of the 68 patients who underwent surgery, 31 (46%) received adjuvant chemotherapy followed by endocrine therapy (tamoxifen and/or letrozole), 15 (22%) received adjuvant endocrine therapy alone, 11 (16%) received adjuvant chemotherapy alone, and 11 (16%) received no adjuvant therapy (Table 1).

Surgical Care

Type of Surgery. Operative reports were not available in BCCOE oncology records. Surgical pathology reports were available for 47 of 68 breast surgeries (69%); of the available reports, 42 (89%) reported at least one lymph node identified in the specimen.

Time to Surgery. Median time to surgery and proportion of patients receiving timely surgery are presented in Table 2. For patients who received no neoadjuvant treatment, median time from biopsy to surgery was 122 days (range 52 – 413); only 8% had surgery within 60 days from biopsy, and 50% experienced a delay of over 120 days from biopsy to surgery. Of note, the median time from biopsy to pathology report in this group was 23 days (0-73); 42% of patients had surgery within 60 days from the date of the pathology report.

For patients who received NAC, median time from last cycle of NAC to surgery was 51 days (range 12-570); 57% had surgery within 60 days from last NAC, and 17% had time to surgery over 120 days from last NAC.

Overall, 32% of patients had surgery within the optimal time frame of 60 days from biopsy (if no neoadjuvant treatments were given) or last cycle of NAC.

Total time from biopsy to surgery for patients who received no neoadjuvant treatments, NAC only, NET only, or NET then NAC in sequence is presented in Appendix A.

Surgical Facility. A minority of surgeries (n=24, 35%) were performed on-site at BCCOE. Most patients (n=42, 62%) received breast surgery at RMH; the remaining two patients had surgery at University Teaching Hospital (CHUK) in Kigali and Kisoro Hospital in Uganda. For patients who received no neoadjuvant treatment, median time from diagnosis to surgery was longer among patients who received surgery at BCCOE (180 days) compared with time from diagnosis to surgery among patients who had surgery at RMH (93 days, p=0.04).
However, among patients who received NAC, the median time from last cycle of NAC to surgery was not statistically significantly different for patients who had surgery at BCCOE (35 days) compared with RMH (67 days; p=0.4).

**Disruptions in Care**

Figure 1 depicts the treatments received and timing of disruptions, progression and loss to follow-up for all patients diagnosed with stage I-III cancer at BCCOE from diagnosis through surgery.

Of the 89 stage I-III patients treated with initial curative intent, 53 (60%) experienced at least one documented disruption in care or became lost to follow-up before receiving surgery. Over half of the 68 patients who ultimately underwent surgery (n=33, 54%) had experienced at least one documented disruption in care prior to surgery.

Twenty-eight of 76 patients referred for surgery (37%) experienced one or more disruptions in care at the point of surgical referral. Seven patients initially referred to BCCOE for surgery were re-referred and underwent surgery at RMH following a disruption in care, and two patients initially referred to RMH underwent surgery at BCCOE.

Fourteen patients (34%) receiving NAC experienced a disruption in scheduled chemotherapy, and 12 patients (32%) receiving NET experienced a disruption in treatment with NET. Thirteen of the 89 patients in our study cohort (15%) experienced treatment disruptions at multiple time points along the pre-operative trajectory of care.

Twenty-six patients had reasons documented in the medical record for disruptions in care. Documented reasons for disruptions in care are shown in Table 3. Patient factors were the most frequently documented reasons, including social and financial issues (n=9), refusing surgery (n=4) and refusing referral for off-site surgery (n=2). Only one treatment disruption was attributed to a patient seeking traditional medicine instead of undergoing surgery. Of the 4 patients documented as refusing surgery, two continued to receive neoadjuvant treatments and ultimately underwent surgery. Clinical indications that resulted in a disruption of care included pregnancy (n=5), chemotherapy toxicity (n=3), referral to RMH for a second opinion when the BCCOE surgeon declined to operate (n=3), and other medical conditions requiring treatment (malaria, thrombocytopenia, and venous thrombosis). System delays due to limited surgeon/operating room availability were documented in the medical record for 5 patients.
DISCUSSION

In this study, we examined barriers to timely surgery among patients diagnosed with breast cancer at the first public cancer referral center in Rwanda and found that only 32% of patients diagnosed with stage I-III breast cancer in 2014-2015 received breast surgery within 60 days of biopsy or last cycle of NAC. This is similar to our findings among patients diagnosed in 2012-2013 (O’Neil, 2017). Disruptions in pre-operative care were common and 13% of patients treated with curative intent were lost to follow-up before receiving surgery. Contrary to our hypothesis, receiving surgery on-site was not associated with shorter time to surgery.

We observed a large difference in rates of timely surgery between patients referred directly from diagnosis (of whom only 8% had surgery within 60 days of biopsy) versus patients referred for surgery after NAC (among whom 57% had surgery within 60 days of last cycle of NAC). Part of this difference is attributable to pathology turnaround times, which extended the time from biopsy to surgery by a median of 23 days for this cohort. Efforts to increase pathology capacity on-site since BCCOE opened in 2012 successfully reduced pathology turnaround time to 5 days for specimens examined on-site at BCCOE as of 2015 (Muvugabiwgi, 2017).

However, the difference in rates of timely surgery persisted when we measured the percentage of patients who received surgery within 60 days of pathology report (42%) versus last cycle of NAC (57%). This may reflect the opportunity for surgical planning and coordination provided during NAC, since surgical evaluation and scheduling may be facilitated concurrently with NAC to reduce wait time for surgery after NAC is complete. Coordinating multidisciplinary care is particularly important when surgical capacity is limited, as is the case at BCCOE.

We had anticipated that receiving surgery at the same facility where diagnosis and neoadjuvant treatments are delivered would be associated with shorter time to surgery. However, in our cohort the opposite was true for patients not receiving neoadjuvant treatment. Patients who received no neoadjuvant treatments and underwent surgery at RMH in Kigali had significantly shorter time to surgery than those who underwent surgery at BCCOE. In contrast, among patients who received NAC, those who underwent surgery at BCCOE had non-significantly shorter time to surgery than those who underwent surgery at RMH.
At BCCOE, the sole general surgeon must appropriately prioritize trauma and acute surgeries over elective cancer surgery. At RMH, greater surgical capacity permits the team of general surgeons to meet acute surgical needs while also prioritizing scheduling of elective cancer surgeries. Although referring patients to another facility for surgery poses challenges for coordination of care, our findings suggest that referring patients for surgery at hospitals with greater surgical capacity may enable more timely scheduling when on-site capacity is limited. Given the significant delays to surgery that we observed, further research with larger sample sizes is needed to assess how centralizing cancer care will impact the timeliness and quality of cancer surgery in LMICs.

**Reasons for Delays and Disruptions in Care**

Among the patients for whom reasons for delays and disruptions were documented, financial and social barriers were common, despite several programs that seek to minimize financial barriers to care at BCCOE, including a robust national health insurance system, free cancer medications and financial support for transportation expenses. This finding is consistent with a study from Haiti demonstrating that high out-of-pocket costs can pose a significant barrier even in settings where cancer care is ostensibly free (O’Neill, 2015).

In our study, 4 patients were documented as refusing recommended breast surgery (5% of those referred). Two of them ultimately underwent surgery, suggesting that with appropriate counseling, patients who initially refuse mastectomy may reconsider. Though traditional medicine is in widespread use in Rwanda, only one patient had a delay attributed to seeking traditional medicine instead of surgery.

Some observed delays were attributed to clinical circumstances requiring changes in treatment protocols, including 5 pregnancies. Pregnancy-associated breast cancer and pregnancies that occur during breast cancer treatment are a particularly significant issue in sub-Saharan Africa, where patients with breast cancer tend to be younger than in high-income countries (Vanderpuye, 2017; Dusengimana, 2018).

**Implications for Strategies to Reduce Delays**

Our findings suggest several opportunities for improving timely access to breast surgery. First, increasing surgical oncology capacity by expanding general surgery capacity at centers like BCCOE or dedicating general surgery resources (e.g., operating room time,
surgeon time, and surgical beds) at referral hospitals to surgical oncology care has potential to reduce wait times for surgery.

Second, efficient treatment planning for multidisciplinary cancer care requires close communication and shared record-keeping between medical and surgical providers, regardless of where surgery is performed. Though our study did not capture direct communication between providers, the lack of surgical records in the oncology records – for example, to confirm the type of surgery performed – limits awareness of surgical care provided. Implementing a system to track patients who are referred to surgery would help identify those who do not receive it and enable timely outreach. BCCOE is transitioning to a more extensive electronic medical record which would facilitate information sharing and examination of the quality of care delivered in the future.

Furthermore, our findings suggest that in settings where limited operative capacity prolongs time to surgery, provision of chemotherapy preoperatively rather than postoperatively can provide time for multidisciplinary coordination and facilitate timely surgery, as long as delays and disruptions in NAC provision are minimized. This strategy of altering treatment sequencing based on local resource constraints has been employed elsewhere to reduce time to treatment initiation (O’Neil, 2018).

Third, pathology services are integral to cancer care and often under-developed in LMICs due to resource and personnel constraints. Reducing pathology turnaround time by increasing local pathology capacity is essential to decrease time to surgery. Our ongoing evaluation of care quality at BCCOE will allow us to investigate the degree to which improved turnaround times in subsequent years facilitate more timely surgery.

Lastly, our study suggests there may be an important role for patient navigation, psychosocial and financial support in minimizing loss-to-follow up and optimizing timely surgery. Peer support and survivor groups for patient education and accompaniment could be one strategy to ease concerns about mastectomy and decrease loss to follow up.

**Future Directions**

Since this project was conducted, clinicians and administrators at BCCOE and RMH have worked together to enhance coordination of care between the two hospitals. BCCOE has replaced the general surgeon on staff with a new surgeon who plans to increase operative capacity at BCCOE through an increased caseload. Lastly, we are working with colleagues
at BCCOE to seek funding for quality improvement initiatives including local capacity-
building and dedicated improvements to surgical workflow.

Limitations

Our study has several limitations. First, the information available in medical records was
often incomplete. Reasons for delays and disruptions were not routinely recorded. Further,
some treatment information was missing from medical records, in part because of care that
occurred in different locations. Thirty-one percent (31%) of charts were missing surgical
pathology reports, and none had operative reports available to verify the type of surgery
performed.

Second, our assessments of timely surgery were limited by the availability of evidence-
based metrics. For example, we were unable to evaluate the timeliness of surgery for the
21% of patients who received only NET. Although there is mounting evidence supporting
use of NET, there is no consensus on the optimal duration of treatment (Spring, 2016).
Further studies to determine the optimal role of NET in breast cancer care in LMICs would
be beneficial. In addition, several patients were classified as having “timely” surgery within
60 days of last NAC yet experienced long disruptions in care before and during neoadjuvant
treatment.

Third, our ability to retrospectively identify reasons for observed delays was limited to the
documentation available in individual patient records. Patient factors and clinical indications
are more likely to be documented than system-related factors. This particularly limited our
understanding of the role of system and facility-related factors.

Finally, our study does not examine the impact of delays on survival. Research is underway
in a larger cohort to examine the impact of breast cancer care quality, including timely
surgery, on breast cancer survival at BCCOE.

CONCLUSION

In this retrospective study of patients with breast cancer at a public Rwandan cancer facility,
we observed frequent delays to surgery, disruptions in care and loss to follow-up during pre-
operative care, particularly at the point of surgical referral. These findings suggest there may
be opportunities to improve breast cancer survival in Rwanda through interventions that
facilitate more timely surgical care.
References


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<td>Not specified (did not return after biopsy)</td>
<td>16</td>
<td>11%</td>
</tr>
<tr>
<td><strong>Breast surgery among patients with stage I-III breast cancer treated with curative intent (n=89)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast surgery received</td>
<td>68</td>
<td>76%</td>
</tr>
<tr>
<td>Surgery recommended but declined by patient</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Lost to follow-up before surgery</td>
<td>12</td>
<td>13%</td>
</tr>
<tr>
<td>Disease progression before surgery</td>
<td>7</td>
<td>8%</td>
</tr>
<tr>
<td><strong>Neoadjuvant and adjuvant systemic treatment among patients who received breast surgery with curative intent (n=68)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant endocrine therapy</td>
<td>29</td>
<td>43%</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>23</td>
<td>34%</td>
</tr>
<tr>
<td>No neoadjuvant therapy</td>
<td>24</td>
<td>35%</td>
</tr>
<tr>
<td>Adjuvant endocrine therapy</td>
<td>46</td>
<td>68%</td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>42</td>
<td>62%</td>
</tr>
<tr>
<td>No adjuvant therapy</td>
<td>11</td>
<td>16%</td>
</tr>
</tbody>
</table>
*includes 2 patients with unknown stage, and 1 patient with stage IV disease who initiated treatment prior to completing staging
†Some patients had more than one neoadjuvant or adjuvant treatment modality
Table 2. Time to breast surgery by surgical facility for patients diagnosed at BCCOE

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Treatment Received Prior to Surgery</th>
<th>Facility</th>
<th>n</th>
<th>Days to Surgery - Median (Interquartile range)</th>
<th>Percentage =&lt;60 days</th>
<th>Percentage =&lt;90 days</th>
<th>Percentage =&lt;120 days</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy to Surgery</td>
<td>None</td>
<td>All</td>
<td>24</td>
<td>122 (76 – 178)</td>
<td>8%</td>
<td>38%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BCCOE</td>
<td>7</td>
<td>180 (147 – 224)</td>
<td>14%</td>
<td>14%</td>
<td>14%</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMH</td>
<td>16</td>
<td>93 (76 – 132)</td>
<td>6%</td>
<td>50%</td>
<td>69%</td>
<td></td>
</tr>
<tr>
<td>End of NAC to Surgery</td>
<td>NAC +/- NET</td>
<td>All</td>
<td>23</td>
<td>51 (30 – 88)</td>
<td>57%</td>
<td>74%</td>
<td>83%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BCCOE</td>
<td>9</td>
<td>35 (31 – 69)</td>
<td>67%</td>
<td>89%</td>
<td>89%</td>
<td>0.41</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RMH</td>
<td>14</td>
<td>67 (28 – 102)</td>
<td>50%</td>
<td>64%</td>
<td>79%</td>
<td></td>
</tr>
</tbody>
</table>

*Wilcoxon rank-sum tests comparing days to surgery among patients who had surgery at BCCOE versus RMH
NAC = neoadjuvant chemotherapy; NET = neoadjuvant endocrine therapy; BCCOE = Butaro Cancer Center of Excellence; RMH = Rwanda Military Hospital
Table 3 – Documented reasons for disruptions in care* (n=44**)

<table>
<thead>
<tr>
<th>Patient factors (n=14)</th>
<th>Financial/social issues</th>
<th>9</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Seeking traditional medicine</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Seeking care abroad</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Patient refused surgery</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Patient refused referral off-site for surgery</td>
<td>2</td>
</tr>
<tr>
<td>System Factors (n=5)</td>
<td>Surgeon/operating room availability</td>
<td>5</td>
</tr>
<tr>
<td>Clinical Indications (n=13)</td>
<td>Management of pregnancy</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Inoperable, referred for 2nd opinion</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy toxicity</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Other medical delay</td>
<td>4</td>
</tr>
<tr>
<td>Unknown (n=27)</td>
<td>Reason not documented</td>
<td>27</td>
</tr>
</tbody>
</table>

*Disruptions in care were defined as events causing delays of >7 days for scheduled neoadjuvant chemotherapy or surgery, >30 days for receipt of neoadjuvant endocrine therapy, any missed visit for surgical evaluation, or any change in clinical status other than progression requiring modification of treatment plan.

**Some patients had multiple disruptions in care and/or disruptions were attributable to multiple factors.
Figure 1 – Timing of Interruption, Progression and LTFU During Pre-Operative Trajectory of Care
Figure 2 – Time from biopsy to surgery among patients treated with curative intent who received no neoadjuvant therapy (n=26), or from last cycle of NAC among patients who received NAC (n=35)

NAC = Neoadjuvant Chemotherapy
Appendix A – Time from Biopsy to Surgery by Pre-Operative Treatment Trajectory

<table>
<thead>
<tr>
<th>Treatment Received Prior to Surgery</th>
<th>n</th>
<th>Median Days to Surgery (Interquartile Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>24</td>
<td>122 (76 – 178)</td>
</tr>
<tr>
<td>Neoadjuvant endocrine therapy only</td>
<td>21</td>
<td>154 (100 – 302)</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy only</td>
<td>15</td>
<td>267 (241 – 392)</td>
</tr>
<tr>
<td>Neoadjuvant endocrine therapy and chemotherapy</td>
<td>8</td>
<td>368 (232 – 551)</td>
</tr>
</tbody>
</table>