A comprehensive approach for quality assessment of breast cancer care

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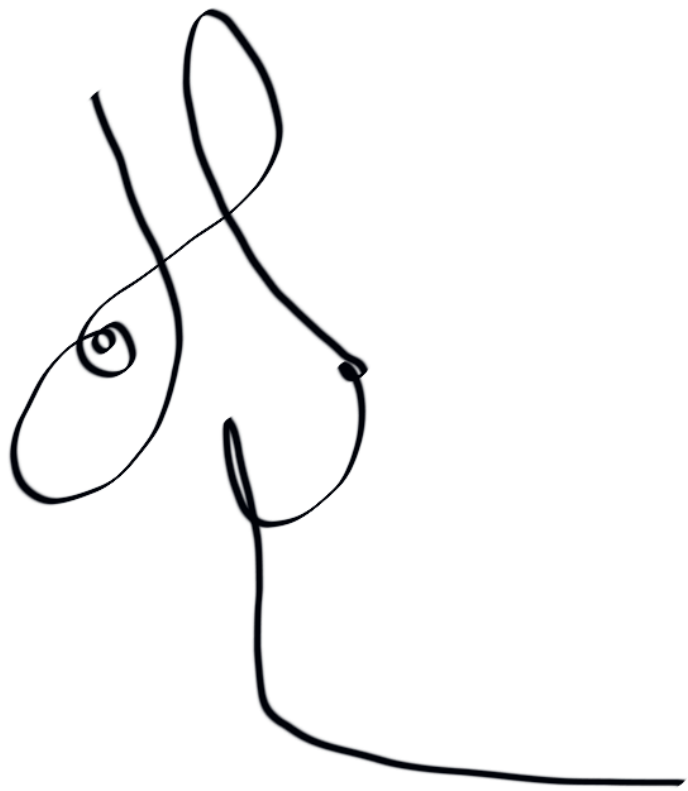
Chapter 10

Summary



Summary

In **Chapter 1**, a general introduction into different dimensions of quality of breast cancer care, and the outline of this thesis is presented. The primary aim of this thesis was to contribute to the improvement of the quality of breast cancer care on an individual and population-based level by using data from multiple nationwide databases. The chapters in this thesis address one or more of the six dimensions of quality of care according to the definition of the Institute of Medicine (*safety*, *effectiveness, patients-centeredness, timeliness, efficiency, and equity*) in each of the chapters.[1] In the first part of this thesis, we analyze the *effectiveness, timeliness* and *efficiency* of preoperative breast cancer care. In the second part, the *safety* and *timeliness* of the adjuvant breast cancer care is investigated and in the concluding part we room for improvement regarding *safety*, *effectiveness* and *efficiency* of different breast reconstructive strategies. Although it seems like the quality dimensions *safety, effectiveness*, *timeliness* and *efficiency* have the largest share in this thesis, *patient-centeredness* and *equity* are strongly connected and hinge on insight into the first four dimensions.

The following conclusions were drawn based on the findings described in the previous chapters of this thesis:

1. A hospital transfer after breast cancer diagnosis is a delaying factor for primary treatment, specifically for those who undergo surgery in the Netherlands.[2]
2. Second opinions in breast cancer care can have a significant impact on diagnostics and primary treatment strategies in certain patients.[3]
3. Immediate breast reconstruction (IBR) after mastectomy is not contra-indicated for the majority of patients who have an indication for adjuvant chemotherapy.[4]
4. Initiation of adjuvant chemotherapy beyond 30 days after surgery is associated with decreased 10-years overall survival in patients with triple-negative breast cancer who undergo breast-conserving surgery (BCS).[5]
5. Direct-to-implant immediate implant-based breast reconstruction (IBBR) compared to two-stage IBBR is associated with a lower unplanned revision incidence.
6. The Netherlands and Denmark have a comparable breast-contour preservation rate around 75%, despite a more frequent use of neoadjuvant chemotherapy and postmastectomy immediate reconstruction in the Netherlands.[6]
7. BCS using oncoplastic techniques is a safe option regarding re-excision and conversion to mastectomy rate.[7]

Part I: Hospital transfer in breast cancer care

There is a large body of literature focusing on factors that influence the continuity of breast cancer treatment.[8-12] Focusing on potential treatment delaying factors may have the potential to improve the quality dimension *timeliness*. A relatively unknown factor in breast cancer care is patients changing hospital after diagnosis,[13] from now on referred to as hospital transfers. **Chapter 2** demonstrated that on a national level almost 5% of the breast cancer patients undergoing primary surgery and almost 25% of those undergoing NAC transferred hospital after diagnosis in the Netherlands.[2] The extent of hospital transfers for both types of treatment decreased between 2014 and 2016. Hospital transfers were more likely in young (aged <40 years) patients and those who underwent a mastectomy with IBR. Time from diagnosis to primary treatment was significantly prolonged up to 9 days after a hospital transfer, specifically for patients undergoing primary surgery. Hospital transfers most commonly occurred if breast cancer had been diagnosed in a district hospital regardless of the primary treatment. While a hospital transfer among patients undergoing primary surgery most commonly occurred towards a teaching hospital, those receiving NAC most commonly changed to another district hospital. Although the extent of hospital transfers among patients who underwent primary surgery was modest, the treatment delaying impact seems substantial.

Part of the extent of hospital transfers may be caused by patients who change hospital due to a second opinion after diagnosis. Evaluating the medical value of breast cancer second opinions could facilitate improvement in *effectiveness* and *efficiency* of the preoperative breast cancer phase. We composed a breast cancer second opinion (BCSO) classification system to quantify the degree of discrepancy in diagnostical findings and treatment proposal between a first and second opinion in a reproducible manner for future studies. **Chapter 3** demonstrated that in more than 45% of breast cancer patients who had not received treatment prior to the consultation a second opinion resulted in at least one minor or major discrepancy in diagnostic findings or treatment proposal.[3] Interestingly, major discrepancies occurred in more than 29% of patients, specifically in the primary treatment proposal (e.g. NAC instead of primary surgery, BCS instead of mastectomy, and in using IBR). Physician and patient initiated second opinions demonstrated to have comparable discrepancy rates. Discrepancy was more common in patients who at the second opinion received additional diagnostics such as imaging or biopsy. The majority of patients did not return to the hospital of first opinion. These findings showed a substantial clinical impact of second opinions and support its use among breast cancer patients. The high-expertise character of the

hospital of second opinion might have influenced our results. Future studies using our classification system are required to answer that question. Improving consensus regarding primary treatment between hospitals might reduce variation between first and second opinion.

Overall, **Part I** of this thesis provided insight into breast cancer patients changing hospital after diagnosis on a nationwide level and on a local level. Moreover, identifying prognostic factors and quantifying the impact of a hospital change on breast cancer care provided insight into the potential room for improvement of *efficiency*, *effectiveness* and *timeliness* of preoperative breast cancer care.

Part II: Continuity of the adjuvant chemotherapy pathway

Despite the vast body of literature, there is an ongoing discussion about the impact of IBR on time from surgery to initiation of adjuvant chemotherapy[14-17] and the time-survival relationship after breast cancer.[15,18-20] While Dutch and European guidelines recommend initiation of adjuvant chemotherapy within 6 weeks after surgery,[21-23] literature shows that the clinical acceptable maximum time between surgery and adjuvant chemotherapy lays between 7 and 12 weeks.[18,20,24] **Chapter 4** demonstrated that while in the Netherlands more than two-third of all patients who received adjuvant chemotherapy after mastectomy received systemic treatment within 6 weeks after surgery, the vast majority within 9 weeks and almost all patients within 12 weeks.[4] Patients undergoing IBR after mastectomy compared to mastectomy alone had a reduced likelihood of receiving adjuvant chemotherapy within 6 weeks, but not within 9 and 12 weeks after limiting confounding by indication by means of propensity score matching. Based on these results, IBR most likely does not delay adjuvant chemotherapy to a clinically relevant extent, suggesting that IBR is not necessarily a contra-indication for patients who undergo a mastectomy and have an indication for adjuvant chemotherapy.

Recent studies suggest that the relationship between time from surgery to adjuvant chemotherapy and survival might be breast cancer sub-type dependent.[20,25-28] Is has been suggested that the clinical acceptable maximum time from surgery to adjuvant chemotherapy might be shorter for more aggressive high-risk tumors, such as triple-negative breast cancer (TNBC). Chapter 5 demonstrated that TNBC patients who underwent BCS and received adjuvant chemotherapy beyond 30 days after surgery had a 69% increased risk of death within 10-years compared to those who received adjuvant chemotherapy within 30 days.[5] No difference in 10-years overall survival (OS)

was observed between the two time-interval groups for patients who underwent mastectomy. Similar associations were observed after stratifying analysis for the use of radiotherapy. Although part of the findings might be explained by residual confounding, these findings support the idea that if chemotherapy is administered in the adjuvant setting, a more timely initiation of chemotherapy in TNBC patients seems warranted after BCS.

After adjusting for confounders, **Part II** of this thesis demonstrated a relatively limited delaying impact of postmastectomy IBR on the continuity of the adjuvant chemotherapy pathway and it highlights the importance of timely initiation of adjuvant chemotherapy in patients diagnosed with TNBC. These findings might be useful for initiatives to improve *timeliness* and *safety* of the quality of adjuvant breast cancer care.

Part III: Quality assessment of breast reconstruction strategies

Previous contradicting studies comparing cosmetic outcomes and complications after immediate IBBR using direct-to-implant and two-stage techniques (tissue expander first) may contribute to unwanted variation in practice among healthcare providers.[29-32] Providing insight into the unplanned revision surgery incidence after both techniques using nationwide data may be used to improve *safety* and *patients-centeredness* of breast reconstruction strategies. **Chapter 6** demonstrated that short- and long-term revision surgery occurred less often after direct-to-implant IBBR compared to two-stage IBBR, although the crude cumulative revision incidence of a long-term revision was comparable after limiting confounding by indication. The majority of revision surgery after two-stage IBBR occurred during the tissue-expander phase. The observed indications for short-term revisions suggest that the rate of revision surgery of both techniques could potentially be improved specifically by optimizing the quality of the mastectomy skin flap and prevention of infections.

Although there is no current golden strategy for the most optimal breast-contour preservation strategy, preservation of the breast mound seems nowadays possible for most early stage breast cancer patients. Breast-contour preservation can be defined using either primary BCS, NAC followed by BCS, or mastectomy followed by IBR.[33] A comparison of these strategies between countries which are comparable regarding their wealth, culture and healthcare organization could provide insight into potential room for improvement of breast cancer care in both countries. In Chapter 7, a substantial difference in breast-contour preservation strategies between Denmark and

the Netherlands was observed, specifically in more common use of NAC followed by BCS and mastectomy followed by IBR in the Netherlands.[6] While the overall breast-contour preservation rate was stable in Denmark between 2012-2017 (75.8% to 76.8%), a significant increase was observed in the Netherlands (69.5% to 78.5%). We observed a decrease in variation between hospitals in breast-contour preservation rates in both countries between 2012 and 2017. Interestingly, a relatively high hospital volume was observed in Denmark compared to the Netherlands. Together with previous chapters, these findings raise the question whether more consensus is warranted among physicians on the different treatment strategies not only on a national, but also on an international level.

Part of the surgical de-escalation and increase in the breast-contour preservation rate might be achieved by optimizing systemic therapies, such as that NAC seems to make some patients eligible for BCS.[34,35] In addition, surgical techniques such as oncoplastic surgery (OPS) during BCS are thought to contribute as well.[36] OPS has the potential to reduce re-excision and conversion to mastectomy rates as OPS has been associated with larger resections while achieving good clinical and patient-reported outcomes.[37-44] Re-excision and conversion to mastectomy after primary BCS are associated with poorer outcomes and additional healthcare costs.[45-47] Chapter 8 demonstrated that patients who underwent primary BCS with OPS compared to BCS only were less likely to undergo re-excision or conversion to mastectomy.[7] Re-excision rates were significantly lower after OPS compared to BCS, although differences were modest. Similar results were found when accounting for the use of boost radiation in patients older than 50 years. Together with previous literature,[38-41,44] these findings support the safe use of OPS, specifically in patients in whom otherwise BCS with a satisfactory cosmetic result would most likely not have been possible.

Part III of this thesis evaluated breast-contour preservation and oncoplastic strategies on a national and international level. The findings can be used to improve quality of breast cancer care, specifically *safety*, *effectiveness* and *efficiency*. The outcomes and identified prognostic factors could be used by physicians during patient-counselling, but also by healthcare policymakers seeking potential room for improvement in current breast reconstructive strategies.

In **chapter 9**, we present a general discussion of the findings of each chapter in which we explore the interpretations, implications, limitations and critically put them in a broader perspective. In conclusion, we elaborate on recommendations for the future perspectives of breast cancer care.

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