Quality assurance in breast cancer care and breast implant surgery

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CHAPTER 9

Summary

SUMMARY

This thesis is about clinical quality audits, used to measure and improve the quality of health care; focusing on the quality of breast cancer care (see: the NBCA) and on the quality of breast implant surgery (see: the DBIR) in the Netherlands.

Evaluation and improvement of the quality of care is of crucial importance in the daily clinical practice, in health insurance and in policymaking. Different tools have been developed to monitor the quality of care, including regulatory inspections, surveys of consumers' experiences, internal assessments and clinical audits.[1] A clinical quality audit is a quality improvement process that seeks to improve patient care and outcomes through a systematic review of care against explicit criteria or standards, established using the principles of evidence-based medicine.[2] The goals of clinical quality audits, in general, are to increase the knowledge about diseases, to improve awareness and understanding of disease and treatment practices and it is an important tool in connecting networks of clinical expertise.

With funding from the Dutch Ministry of Health, the Association of Surgeons of the Netherlands (ASN) proceeded to develop the first national clinical quality audit in the Netherlands in 2009: the Dutch Surgical Colorectal Audit (DSCA).[3] Subsequent to the success of the DSCA, the Dutch Institute of Clinical Auditing (DICA) was founded in 2011 with the objective to facilitate the start-up of new nation-wide clinical audits in the Netherlands.[4] Concurrently, the Dutch Health Care Inspectorate observed a high rate of tumor-positive margins after breast-conserving surgery in a number of hospitals in the Netherlands, which confirmed the need for a national audit for the monitoring of the quality of breast cancer care.[5] In 2011, the NABON Breast Cancer Audit (NBCA) was instituted as a nation-wide audit to address the quality of breast cancer care in the Netherlands.[6] Meanwhile, more than 100.000 newly diagnosed patients treated for breast cancer have been registered. And within 7 years auditing, multiple processes and outcome measures (quality indicators) that cover different aspects of the multidisciplinary care path for breast cancer patients have been evaluated in order to examine improvement. Subsequently, new audit initiatives and quality assurance programs for other diseases have been developed and rapidly emerging in the Netherlands (21 audits facilitated by DICA today including the DBIR).[7]

Part I: Quality assurance in breast cancer care; the NABON breast cancer audit (NBCA)

Breast cancer is the most common cause of cancer among women. In the Netherlands over 15.000 women get diagnosed with breast cancer every year.[8] Over the past decades, many refinements of treatment modalities have been widely implemented in the field of breast cancer. In order to monitor the quality of the delivered breast cancer care, the NBCA audit was founded by clinicians of different disciplines involved in breast cancer.

In **chapter 2**, we focused on trends in the use of Neoadjuvant Chemotherapy (NAC) in breast cancer treatment. Chemotherapy is timed either prior to or following surgery, respectively neoadjuvant (NAC) or adjuvant (AC), both leading to similar disease-free and overall survival.[10,11] Chemotherapy intents to eliminate potential existing micro metastases, thus decreasing recurrence rates and mortality.[9]

NAC has several benefits compared to AC. Firstly, NAC aims to downsize the tumour to improve the possibility of a radical resection or to enable breast conservation surgery.[12,13] Another benefit of NAC includes the opportunity to de-escalate surgical treatment of the axilla.[14,15] Other potential advantages of NAC include the opportunity to investigate tumor biology, to monitor response and adapt to suboptimal response. Moreover, it is demonstrated that NAC, when compared to adjuvant chemotherapy, may even improve survival in triple-negative and HER2 positive BC subtypes when a pathological complete response (pCR) is achieved.[16]

In accordance with international guidelines, the Dutch national breast cancer guideline recommends NAC for patients with stage III BC aged <70 years. From 2011 to 2015, a high consistent rate of NAC (77%) was observed in our population of women aged 18-70 years with stage III BC, However, inter-hospital variation in the rate of NAC use was noticed varying between 0 % to 100%. We found the following predictive patient and tumour factors for the use of NAC in patients with breast cancer: young age, large tumour size, advanced nodal disease, and a negative hormone receptor status. After adjustment for these predictive factors known, the variation between the 89 Dutch hospitals remained, which indicates other potential factors of influence. Of notice, we

observed a significantly higher use of NAC in hospitals participating in neoadjuvant clinical studies (83% versus 73%).

In **chapter 3,** we evaluated the opinion of surgical and medical oncologists on the use of NAC for breast cancer. Clinicians (70 surgical and 68 medical oncologists) participating in breast cancer care in the Netherlands completed a 20-question online survey on the influence of patient, disease, and management related factors on their decisions towards NAC. NAC was recommended for locally advanced breast cancer according to most of the clinicians (94%). Despite the willingness to downstage (75%), only 64% of clinicians stated that they routinely recommended NAC when systemic therapy was indicated preoperatively. Concerns that prevented clinicians from recommending NAC are: comorbidities, age >70 years, and WHO-performance status ≥ 2. Opinions on surgical management after NAC were inconclusive; while 75% recommends NAC to enable BCS, some stated that BCS after NAC increases the risk of a non-radical resection (21%), surgical complications (9%) and recurrence of disease (5%).

In **chapter 4**, we gain insight into patients' experiences with decisions on the timing of chemotherapy. A 35-item online questionnaire was distributed among female patients (age>18) treated with either NAC or AC for stage II and III breast cancer, and almost 400 responded. Outcome measures were the experienced exchange of information on the possible choice between both options and patients' involvement in the final decision on chemotherapy timing. The need to make a treatment decision on the timing of their chemotherapy (NAC or AC) was found to be made explicit in only a small number of adjuvant treated patients, in particular in breast cancer stage II. Less than half of the respondents felt they had a real choice.

In **chapter 5**, we analyzed trends in the use of neoadjuvant chemotherapy (NAC) and the impact on surgical outcomes (in terms of positive margins and re-operations). Between 2011 and 2016, the use of NAC in the Netherlands increased from 9% to 18%. Coinciding with this trend, we demonstrated that NAC increases the rates of breast-conserving surgery (BCS) for all stages of breast cancer from 43% in 2011 to 57% in 2016. The overall positive margin rate in our study is 6,9% for 'BCS after NAC' compared to 3,3% for 'primary BCS', leading to a re-operation rate of 6,6% in 'BCS after NAC' and 5,3% in 'primary BCS'. Moreover, this nationwide data showed that

'BCS after NAC' compared to 'primary BCS' results in equal surgical outcomes for cT2 invasive breast cancer and improved surgical outcomes for cT3 invasive breast cancer. In view of the trend towards de-escalation of surgical treatment in selected patients with an excellent pathologic response, these promising results confirm that clinicians are increasingly able to perform 'BCS after NAC'.

In **chapter 6**, we evaluated the management of axillary lymph-node positive breast cancer in the Netherlands. Axillary lymph node management in breast cancer patients has changed dramatically during past decades. Previously, performing an axillary lymph node dissection (ALND) was the standard of care for all non-metastatic breast cancer patients. However, ALND is associated with a significant risk of complications such as arm swelling (lymphedema), pain, restricted shoulder movement, and sensory changes in the arm and hand.[17,18] In the early 90s, sentinel lymph node biopsy (SLNB) was introduced as an accurate and less invasive axillary staging procedure, omitting the need for ALND in early-stage sentinel lymph node-negative breast cancer patients.

Since the publication of the results of the ACOSOG-Z0011 and AMAROS trial, omitting a ALND in sentinel node-*positive* breast cancer patients is proposed in selected patients.[19,20,21,20] The results of these trials are illustrated by the 2012 Dutch breast cancer guideline, suggesting omission of ALND in cT1-2N0 breast cancer patients with a maximum of two positive sentinel nodes treated with breast conserving treatment and adjuvant systemic therapy.[22]

Between 2011 and 2015, the use of sentinel lymph node biopsy as definitive axillary staging increased from 92% to 98% for all breast cancer patients. ALND as definitive axillary staging decreased from 24% to 6%. This decreasing trend in the numbers of ALNDs for *all* tumour stadia might reflect the growing experience and the confidence among clinicians in the Netherlands towards less extensive axillary surgery of sentinel node-positive breast cancer.

Part II: Quality assurance in breast implant surgery; the Dutch Breast Implant Registry (DBIR)

Breast augmentation is the most commonly performed surgical procedure in plastic surgery worldwide. Most of the procedures performed are for cosmetic purposes, a smaller part for breast reconstructive reasons. In the Netherlands, approximately 3.3% of all mature women have breast implants.[23]

Although the use of breast implants is generally considered to be safe, breast implants are associated with short- and long-term complications, such as infection, implant rupture or deflation, late seroma, and capsular contracture.[24,25,26] In particular, implant scandals from the Dow-Corning crisis in the 1980s to the more recent PIP crisis have raised public awareness.[27] Recently, an association between breast Anaplastic Large Cell Lymphoma (ALCL) has been found.[28,29] Furthermore, it has been suggested that there is an association between autoimmunity and silicon exposure resulting in ASIA (autoimmune/inflammatory syndrome induced by adjuvants) and various autoimmune diseases.[30,31,32]

In response to these emerging safety concerns, several national societies around the world developed breast devices registries of which six up and running registries today, including the Australian Breast Device Registry (ABDR),[33] the Bröstimplantatregistret of Sweden (BRIMP),[34] the Austrian Breast Implant Register (ABIR),[35] the Breast and Cosmetic Implant Registry of the United Kingdom (BCIR),[36] the US National Breast Implant Registry (NBIR)[37], and the Dutch Breast Implant Registry (DBIR).[38]

The DBIR registry was founded in 2015, with the objective to facilitate and organize the initiation of nationwide breast implant-related outcome measures in the Netherlands. A unique feature of the DBIR is its opt-out construct, without the need for informed consent. The national coverage has been assessed by comparing the number of institutions in DBIR to the number of eligible institutions known by the Dutch Health and Youth Care Inspectorate (IGJ). In the first full registration year (2016), the participation rate was 95% for hospitals and 78% for private clinics.

In **chapter 7**, we provide an overview of early outcomes and experiences of the DBIR registry. Between 2015 and 2017, a total of 15,049 patients and 30,541 breast implants

were included. A minimum incidence rate of 1 implant per 1,691 women in 2017 could be determined. The majority of devices was inserted for a cosmetic indication 26,036 (85.2%), and 4,505 (14,8%) for a breast reconstruction. In general, patient, device and surgery characteristics differed per indication group. Patients who underwent cosmetic breast augmentation were younger than breast reconstruction patients (31,5 versus 49,7 years of age). Between 2016 and 2017, a decrease in the use of textured implants was seen in both indication groups. Furthermore, in the reconstructive group, an increase of the use of round implants and silicone filled implants was found, with appears to coincide with the critical issue of breast implant-associated ALCL.

Another preliminary finding is the differences between hospitals in the use of four selected perioperative infection control measures (all ranged 0-100%). Overall, an increased use was shown of prophylactic intravenous antibiotics, gloves change before the insertion, and in the rinse of a breast implant with an antiseptic solution. The use of drains decreased in reconstructive procedures but increased in cosmetic augmentations. Long-term clinical data will eventually reveal the actual health effects of intraoperative techniques and antiseptic precautions.

In the final part of this thesis, **chapter 8**, we have outlined the process undertaken by the International Collaboration of Breast Registry Activities (ICOBRA). ICOBRA is an international multidisciplinary group with expertise in breast device registries including consumer representatives, national regulators, and biostatisticians, and were gathered to develop a standardized global minimum dataset for breast implant registries. Data points from the six up and running national breast implant registries were compared. Secondly, a modified Delphi approach was used, with surveys requiring the panellists to rate the importance of each data point to be included in the global minimum data set. After four survey rounds, a consensus was reached on a list of 32 data points to be included in the global core dataset. Data points for which consensus was not achieved (16 data points), were not voted into the core set and became the optional dataset. Consensus on definitions for all data points was achieved using the definitions of the Australian dataset as the starting point. The ICOBRA core- and optional dataset is almost completely integrated into the DBIR dataset. It is expected that the global dataset will be adopted by currently operating breast device registries within two years and by all new breast implant registries in the ICOBRA network (including Australia,

Austria, Canada, France, Germany, Ireland, Italy, the Netherlands, New Zealand, South Africa, the United Kingdom, and the United States). The ICOBRA global dataset will allow pooling data from breast implant registries in order to evaluate active surveillance and comparative outcomes. This will safeguard the health of recipients of breast implants by preventing implantation of under-performing devices.

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