



DUTCH
INSTITUTE
FOR CLINICAL
AUDITING

Goedgekeurde aanvraag gegevens ten behoeve van wetenschappelijk onderzoek

NBCA201802 Heeg

Datum

Oktober 2018

Titel onderzoek

Impact of immediate breast reconstruction after mastectomy on the timing of adjuvant chemotherapy: a nationwide study in the Netherlands'

Contactpersoon

Erik Heeg, arts-onderzoeker NBCA, DICA, Leiden

Aanvragersgroep

E. Heeg, arts-onderzoeker NBCA, DICA

X. Harmeling, arts-onderzoeker Erasmus MC, Erasmus MC

B. Becherer, dagelijks uitvoerende arts-onderzoeker, DICA

M.J. Vrancken Peeters, oncologisch chirurg AvL, voorzitter NBCA, Antoni van Leeuwenhoek ziekenhuis (AvL)

M.A.M. Mureau, hoofd onderzoek, plastisch chirurg Erasmus MC, bestuurslid NBCA, Erasmus MC

Beschrijving onderzoek

Despite advancements in diagnostics and systemic treatment, up to one-third of breast cancer patients undergoes a mastectomy as their first surgical treatment to achieve local control of the disease (1). Additionally, chemotherapy plays an essential role in the adjuvant therapy of breast cancer. The European Society for Medical Oncology (ESMO) recommends starting AC within 2-6 weeks (13) and the Dutch Plastic Surgery Association recommends within six weeks after surgery. A considerable amount of research has been published on the relationship of time from surgery to adjuvant chemotherapy (AC) and survival of breast cancer patients. Several studies have reported that initiation of AC within 6 to 12 weeks after surgery decreased the disease-free and overall survival (2-9) and is clinically acceptable. Although no international consensus exists on the definition of an unacceptable delay, it is advocated in all guidelines that initiation of AC should not be unnecessarily delayed as it has a negative impact on survival, especially patients at higher risk of recurrence (5, 6, 12). One of the current discussions in minimizing unnecessary delay is the impact of immediate breast reconstruction (IBR) after mastectomy as a treatment delaying factor. There has been a growing concern regarding this impact as an increasing number of patients underwent IBR in the last decade (14, 15). Breast reconstruction can be performed immediately after mastectomy or delayed after completion of additional treatment. Due to lack of high-level evidence and conflicting conclusions in literature physicians are cautious to recommend IBR if adjuvant chemotherapy is part of the treatment plan preoperatively (16).

Loss of the breast after surgery can negatively affect the body image, sexuality, and self-esteem of a woman (17). IBR aims to improve these adverse effects and increase the quality

2017.1



DUTCH
INSTITUTE
FOR CLINICAL
AUDITING

of life. Despite the longer operation time, IBR has been reported to achieve excellent aesthetic results and a less psychological impact for the patient in comparison to delayed reconstruction due to fewer operations and hospital admissions (18, 19). Furthermore, previous studies reported that no contraindications exist for IBR concerning the number of adverse events in comparison to mastectomy alone in combination with adjuvant chemotherapy (20-23).

A systematic review from 2015 concluded that IBR does not delay the time to adjuvant chemotherapy (TTC) to a clinical extent, although the included studies showed strong contradictory results and the clinical limit was set at more than 12 weeks (24). The current literature on this topic exists of single-center studies with statistically heterogenic approaches. A nationwide study with an analysis that adjusts for the treatment by indication bias could provide the answer if IBR is an unnecessary treatment delaying factor.

Research aim:

This study aims to analyze whether IBR negatively affects the TTC compared to mastectomy only on a nationwide scale in the Netherlands.

1. hTTCs://dica.nl/jaarrapportage-2016 Leiden, Netherlands: Dutch Institute for Clinical Auditing; 2016 [Available from: hTTCs://dica.nl/jaarrapportage-2016.
2. Yu KD, Fan L, Qiu LX, Ling H, Jiang YZ, Shao ZM. Influence of delayed initiation of adjuvant chemotherapy on breast cancer survival is subtype-dependent. *Oncotarget*. 2017;8(28):46549-56.
3. Chavez-MacGregor M, Clarke CA, Lichtensztajn DY, Giordano SH. Delayed Initiation of Adjuvant Chemotherapy Among Patients With Breast Cancer. *JAMA Oncol*. 2016;2(3):322-9.
4. Cold S, Düring M, Ewertz M, Knoop A, Møller S. Does timing of adjuvant chemotherapy influence the prognosis after early breast cancer? Results of the Danish Breast Cancer Cooperative Group (DBCG). *Br J Cancer*. 2005;93(6):627-32.
5. Farolfi A, Scarpi E, Rocca A, Mangia A, Biglia N, Gianni L, et al. Time to initiation of adjuvant chemotherapy in patients with rapidly proliferating early breast cancer. *Eur J Cancer*. 2015;51(14):1874-81.
6. Gagliato DeM, Gonzalez-Angulo AM, Lei X, Theriault RL, Giordano SH, Valero V, et al. Clinical impact of delaying initiation of adjuvant chemotherapy in patients with breast cancer. *J Clin Oncol*. 2014;32(8):735-44.
7. Lohrisch C, Paltiel C, Gelmon K, Speers C, Taylor S, Barnett J, et al. Impact on survival of time from definitive surgery to initiation of adjuvant chemotherapy for early-stage breast cancer. *J Clin Oncol*. 2006;24(30):4888-94.
8. Alderman AK, Collins ED, Schott A, Hughes ME, Ottesen RA, Theriault RL, et al. The impact of breast reconstruction on the delivery of chemotherapy. *Cancer*. 2010;116(7):1791-800.
9. Downing A, Twelves C, Forman D, Lawrence G, Gilthorpe MS. Time to begin adjuvant chemotherapy and survival in breast cancer patients: a retrospective observational study using latent class analysis. *Breast J*. 2014;20(1):29-36.
10. Yu KD, Huang S, Zhang JX, Liu GY, Shao ZM. Association between delayed initiation of adjuvant CMF or anthracycline-based chemotherapy and survival in breast cancer: a systematic review and meta-analysis. *BMC Cancer*. 2013;13:240.
11. Raphael MJ, Biagi JJ, Kong W, Mates M, Booth CM, Mackillop WJ. The relationship between time to initiation of adjuvant chemotherapy and survival in breast cancer: a systematic review and meta-analysis. *Breast Cancer Res Treat*. 2016;160(1):17-28.
12. Zhan QH, Fu JQ, Fu FM, Zhang J, Wang C. Survival and time to initiation of adjuvant chemotherapy among breast cancer patients: a systematic review and meta-analysis. *Oncotarget*. 2018;9(2):2739-51.



DUTCH
INSTITUTE
FOR CLINICAL
AUDITING

13. Senkus E, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, et al. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2015;26 Suppl 5:v8-30.
14. (DICA) DIfCA. Jaarrapportage 2016 2016 [Available from: [hTTCs://dica.nl/media/993/DICA-2016-jaarverslag.pdf](https://dica.nl/media/993/DICA-2016-jaarverslag.pdf)].
15. Liederbach E, Sisco M, Wang C, Pesce C, Sharpe S, Winchester DJ, et al. Wait times for breast surgical operations, 2003-2011: a report from the National Cancer Data Base. *Ann Surg Oncol.* 2015;22(3):899-907.
16. Wanzel KR, Brown MH, Anastakis DJ, Regehr G. Reconstructive breast surgery: referring physician knowledge and learning needs. *Plast Reconstr Surg.* 2002;110(6):1441-50; discussion 51-4.
17. Gopie JP, Hilhorst MT, Kleijne A, Timman R, Menke-Pluymers MB, Hofer SO, et al. Women's motives to opt for either implant or DIEP-flap breast reconstruction. *J Plast Reconstr Aesthet Surg.* 2011;64(8):1062-7.
18. Gerber B, Marx M, Untch M, Faridi A. Breast Reconstruction Following Cancer Treatment. *Dtsch Arztebl Int.* 2015;112(35-36):593-600.
19. Agrawal A, Sibbering DM, Courtney CA. Skin sparing mastectomy and immediate breast reconstruction: a review. *Eur J Surg Oncol.* 2013;39(4):320-8.
20. El-Sabawi B, Sosin M, Carey JN, Nahabedian MY, Patel KM. Breast reconstruction and adjuvant therapy: A systematic review of surgical outcomes. *J Surg Oncol.* 2015;112(5):458-64.
21. Warren Peled A, Itakura K, Foster RD, Hamolsky D, Tanaka J, Ewing C, et al. Impact of chemotherapy on postoperative complications after mastectomy and immediate breast reconstruction. *Arch Surg.* 2010;145(9):880-5.
22. Oh E, Chim H, Soltanian HT. The effects of neoadjuvant and adjuvant chemotherapy on the surgical outcomes of breast reconstruction. *J Plast Reconstr Aesthet Surg.* 2012;65(10):e267-80.
23. Tanaka S, Hayek G, Jayapratap P, Yerrasetti S, Hilaire HS, Sadeghi A, et al. The Impact of Chemotherapy on Complications Associated with Mastectomy and Immediate Autologous Tissue Reconstruction. *Am Surg.* 2016;82(8):713-7.
24. Xavier Harmeling J, Kouwenberg CA, Bijlard E, Burger KN, Jager A, Mureau MA. The effect of immediate breast reconstruction on the timing of adjuvant chemotherapy: a systematic review. *Breast Cancer Res Treat.* 2015;153(2):241-51.