Surgical trauma and postoperative immune suppression in breast-conserving surgery versus mastectomy: a pilot study

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Comparing the release of DAMPs and subsequent immune suppression after breast-conserving surgery versus mastectomy.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Observational invasive

Summary

ID

NL-OMON48770

Source
ToetsingOnline

Brief title
BREAST

Condition

- Breast neoplasms malignant and unspecified (incl nipple)
- Breast therapeutic procedures

Synonym
Breast surgery, mamma surgery

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Breast-conserving surgery, DAMPs, Immune suppression, Mastectomy

Outcome measures

Primary outcome

o Plasma concentration of DAMPs (nDNA, mtDNA, HMGB-1 and HSP70) and cytokines

(TNF*, IL6 and IL10)

o Ex vivo leucocyte responsiveness: IL-6 and IL-10 production upon LPS

stimulation

o HLA-DR mRNA expression as a measure of immune suppression

o Serum soluble PD-L1

Secondary outcome

Not applicable

Study description

Background summary

Despite extensive research, breast cancer is still the number one cause of cancer-related deaths in women. The landmark trials of the 1980s revealed that survival after breast-conserving surgery followed by radiation treatment (RT) is similar to survival after radical mastectomy. At that time, radiation, chemotherapy and endocrine therapy were infrequently used. Over the last years, several large population based retrospective trials investigated whether survival between breast conserving surgery and mastectomy remains comparable with the current treatments and expertise. However, most of these trials report superior survival in the breast-conserving surgery group when compared to mastectomy. This discovery is not geographically bound (Denmark, Norway, California, the Netherlands), not age dependent and corrected for all tumour- and patient variables available in the cancer registration database. There is no straightforward explanation as to why limited surgery for early stage breast cancer could be superior to mastectomy. A possible contributing factor is

radiotherapy, as the majority of breast-conserving surgery patients receive radiotherapy in contrast to few patients after mastectomy. Undoubtedly, on the other hand, there is a larger degree of surgical trauma in mastectomy, which is associated with more complications. A plausible hypothesis emerging in recent literature is that more extensive surgical trauma leads to an altered immune response. Uncontrolled damage to cells as occurs during trauma or surgery leads to the release of danger-associated molecular patterns (DAMPs), substances that are either actively released by cells under threat, or components of the cell or extracellular matrix that are exposed upon cell damage. These DAMPs function as ligands for immune receptors that, upon binding, induce an anti-inflammatory immune response characterized by the release anti-inflammatory interleukin-10 (IL-10), decreased monocytic HLA-DR expression and reduced production of pro-inflammatory cytokines TNFa and IL-6 upon ex vivo lipopolysaccharide (LPS) stimulation. Fragidiakis et al describe a strong correlation between immune status and recovery from surgery. In trauma patients, the suppressed immune state has been linked to infectious complications and mortality. Moreover, a recent study by Máca et al. shows DAMPs reflect the degree of surgical trauma and predict morbidity and mortality after major abdominal surgery. Several studies suggest a relationship between postoperative complications and the eventual incidence of metastasis. However, comparing study results remains challenging due to heterogeneity in reports and no clear definition of complications. This pilot study will further explore the role of DAMPs and immune suppression after breast cancer surgery. We hypothesize that more extensive surgical trauma of mastectomy is associated with a higher release of DAMPs and subsequent immune suppression, which in turn may lead to postoperative complications.

Study objective

Comparing the release of DAMPs and subsequent immune suppression after breast-conserving surgery versus mastectomy.

Study design

A mono-centre prospective observational pilot study (n=40)

Study burden and risks

Patients already scheduled to undergo either breast-conserving surgery or mastectomy will be asked to participate in the study, participating does not alter or delay their treatment in any way. If a patient decides to participate, a small amount of blood will be collected before surgery, 1 hour- and 1 day after surgery. Where possible, this will be combined with routine laboratory assessment to avoid unnecessary extra vena puncture. Baseline-, tumour- and treatment characteristics, perioperative parameters and complications will be

extracted from the patient*s medical file only with informed consent.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Female
- Age * 18 years
- Undergoing breast conserving surgery or mastectomy
- Obtained informed consent

Exclusion criteria

- <18 years old
- No informed consent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-06-2020
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	19-12-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-03-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65918.091.18