

Axillary Node Clearance

Tuomo J. Meretoja

- 24.1 Introduction (History and Rationale for Axillary Clearance) – 286**
- 24.2 Indications for Axillary Clearance – 286**
 - 24.2.1 Staging – 286
 - 24.2.2 Preoperatively Detected Axillary Metastases – 286
 - 24.2.3 Sentinel Node Metastasis – 286
- 24.3 Anatomy of the Axilla – 287**
- 24.4 Surgical Technique of Axillary Clearance – 288**
- 24.5 Pathological Analysis – 289**
- References – 290**

24.1 Introduction (History and Rationale for Axillary Clearance)

Axillary clearance (AC) and axillary lymph node dissection (ALND) are synonyms for the removal of an anatomically defined area of axillary fat which contains the axillary lymph nodes. Historically, AC was the only method for staging the axilla and was performed in all breast cancer patients prior to the SLNB era. A historical landmark trial, the NSABP B04, randomized breast cancer patients to AC vs. no axillary surgery and concluded that AC in clinically node-negative breast cancer patients was purely a staging procedure with no impact on survival [1]. However, this study was considered underpowered to detect a small survival benefit from AC. A later meta-analysis of six historical randomized trials from 1951 to 1987 comparing breast cancer surgery with or without AC concluded that prophylactic AC conferred an average 5.4% survival benefit [2]. All of these studies were conducted prior to modern adjuvant therapies, and thus the survival benefit from AC in modern clinically node-negative patient material is unclear.

Axillary clearance, both in clinically node-negative and node-positive breast cancer patients, provides accurate staging information by indicating the total number of tumour-positive and tumour-negative axillary lymph nodes.

24.2 Indications for Axillary Clearance

24.2.1 Staging

The indications for AC as a staging procedure in clinically node-negative breast cancer are currently very limited, as SLNB has almost completely replaced AC due to its reduced morbidity. Failure to detect the sentinel node occurs in approximately 2% of patients. There is no robust evidence on the preferred staging procedure of these patients, and the options include a level I or level I–II AC or a four-node sample, which is mainly used in the UK. One needs to keep in mind that failure to localize the sentinel node intraoperatively may be due to gross axillary tumour burden [3].

In addition, there are subgroups of breast cancer patients in whom SLNB is not recommended as a staging procedure due to a lack of evidence of accuracy. Inflammatory breast cancer and locally advanced breast cancer are both, typically, administered neoadjuvant or primary systemic chemotherapy followed by surgery, and axillary management in the neoadjuvant setting is covered in a later chapter (► Chap. 25) [4]. If primary surgical treatment is planned due to contraindications for primary systemic chemotherapy, AC is the preferred staging procedure both in inflammatory and locally advanced breast cancer, even if clinically node negative [5]. Furthermore, the American Society of Clinical Oncology (ASCO) Clinical Practice Guideline recommends performing an AC as the staging procedure in pregnant women with breast cancer, due to a lack of evidence for SLNB in this set-

ting [5], whereas European practice guidelines do not consider pregnancy a contraindication for radiotracer-based SLNB [6]. Nevertheless, there is national and local variance in SLNB contraindications.

An algorithm summarizing standard axillary management is shown below (► Fig. 24.1).

24.2.2 Preoperatively Detected Axillary Metastases

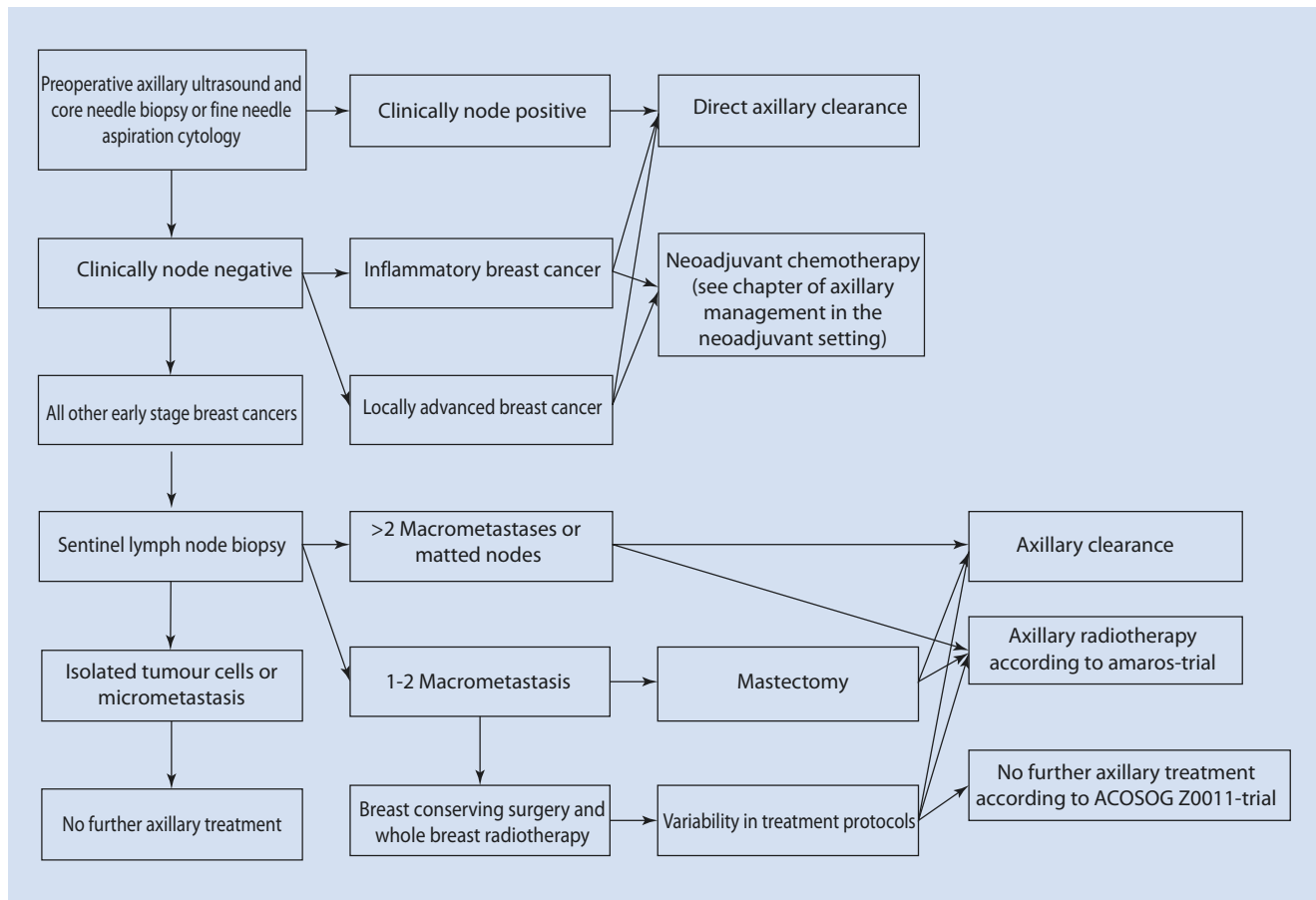
A direct AC without SLNB remains the standard of care in clinically node-positive breast cancer patients, with preoperatively detected axillary lymph node metastases [5, 7]. In these patients, AC provides accurate knowledge of the total number of metastatic lymph nodes, which is an important prognostic indicator, although it may not have much value in adjuvant therapy decision-making [8].

The high sensitivity of modern preoperative axillary ultrasound may detect single axillary metastases even with no suspicious nodes on palpation, which poses an obvious overlap with the patient population with SLNB-detected axillary macrometastasis. This overlap and inconsistency in treatment protocols (see ► Chap. 23 on SLNB) is the subject of ongoing research. In patients with preoperatively detected high-volume tumour burden in the axilla, primary systemic chemotherapy is commonly considered.

24.2.3 Sentinel Node Metastasis

The matter of the tumour-positive sentinel node is covered in detail in ► Chap. 23. In summary, axillary clearance is not indicated in cases with tumour-negative sentinel nodes. Similarly, neither isolated tumour cells nor micrometastasis in the sentinel node is usually considered an indication for axillary clearance [5, 9]. However, in cases of macrometastatic sentinel node(s), there is considerable variation in treatment protocols between countries and centres with many centres adopting individualized treatment algorithms based on patient-specific characteristics and multidisciplinary team evaluations.

A number of risk prediction tools and nomograms have been published to evaluate the patient-specific risk of additional metastases or N2 disease risk after tumour-positive sentinel node findings [10–12]. Many of these prediction tools are published as online calculators that provide the patient-specific risk as a risk percentage. Such aids may be used in the decision-making process for AC after finding a metastatic sentinel node. Nonetheless, there is no consensus on clinically applicable risk thresholds for non-sentinel node metastases or N2 disease that would indicate the need for AC or axillary radiotherapy. Furthermore, the accuracy and performance of a specific prediction model should be assessed and validated for use in each centre before adoption into clinical practice.



■ Fig. 24.1 Algorithm summarizing standard axillary management

24.3 Anatomy of the Axilla

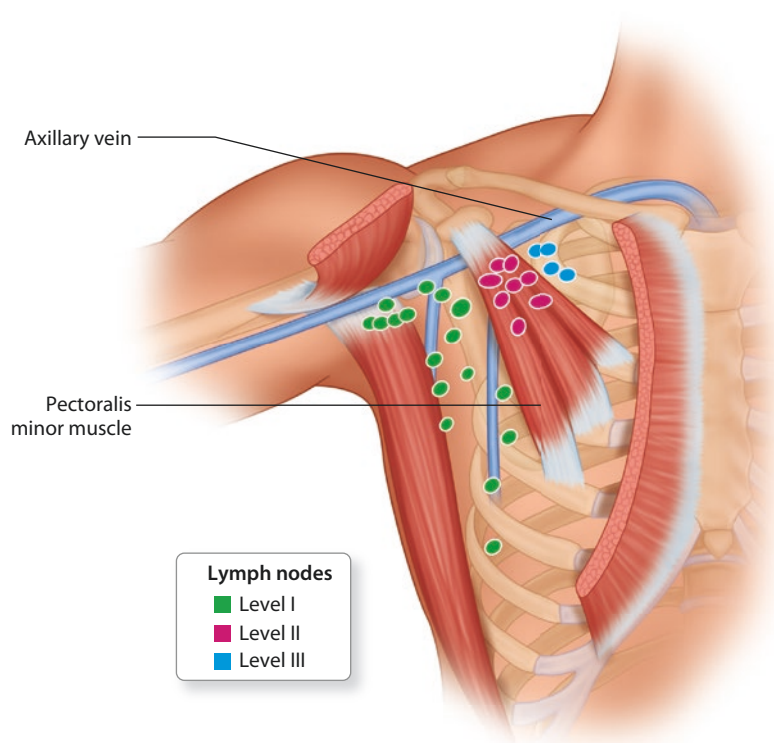
The axillary lymph node basin is a triangular space bordered laterally by the latissimus dorsi muscle, medially by the serratus anterior muscle and the thoracic wall, cranially by the axillary vein, anteriorly by the pectoralis major and minor muscles and posteriorly by the latissimus dorsi, teres major and subscapularis muscles.

The axillary lymph nodes are divided into three anatomical levels according to Berg [13]: Level I lymph nodes are located lateral to the pectoralis minor muscle, whereas level II lymph nodes are posterior, and level III lymph nodes are medial to the pectoralis minor muscle (■ Fig. 24.2).

The axillary lymph nodes are surrounded by axillary fat, which is also crossed by a number of nerves and vascular structures. The long thoracic nerve is the motor nerve of the serratus anterior muscle. It lies deep in the axilla running in a cranio-caudal direction along the serratus anterior muscle, lateral to the chest wall. Damage to the long thoracic nerve may cause paresis to the serratus anterior muscle, which can be clinically manifest by ‘winging of the scapula’. The thoracodorsal bundle includes the motor nerve, artery and vein

which supply the latissimus dorsi muscle. The thoracodorsal bundle crosses the axillary fat lateral to the long thoracic nerve. The vein of the bundle intersects with the axillary vein at the cranial border of the axilla, whereas the nerve and the artery dive posterior to the axillary vein. The intercostobrachial nerve(s) is a sensory nerve innervating a variable area of the skin of the dorsum of the upper arm. Generally the nerve(s) branches from the intercostal nerves and runs through the serratus anterior muscle, crosses the level I axillary fat parallel but caudally to the axillary vein and enters the arm. However, there is substantial anatomical variation in the course and branching of this nerve [14–16]. Damage or transection of the intercostobrachial nerve causes variable sensory changes to the area it innervates. The lateral thoracic vein and artery run along the serratus anterior muscle, anteriorly to the long thoracic nerve. The medial pectoral pedicle comprises the medial pectoral nerve and accompanying vascular vessels. It is located at the lateral border of the pectoralis minor muscle. The medial pectoral nerve innervates both pectoralis minor and part of the pectoralis major muscles. Damage to the medial pectoral pedicle therefore may cause paresis of the pectoralis muscles [17].

Fig. 24.2 Axillary lymph node levels I–III, according to Berg



24.4 Surgical Technique of Axillary Clearance

When axillary clearance is indicated in breast cancer patients, a dissection of Berg levels I and II should be conducted as routine. If clinically suspicious nodes are palpable medial to level II, level III should also be cleared, although this is often done as routine. Generally, if axillary clearance is performed, all clinically suspicious nodes should be removed, and sometimes neurovascular structures may have to be sacrificed in order to achieve radical removal of all cancerous tissue.

There is undoubtedly abundant variation in the surgical technique in dissecting the axillary lymph nodes. The dissection can be performed either via the same incision as the breast operation, such as mastectomy or lateral breast-conserving surgery, or through a separate incision to the axilla. The dissection is typically begun from the caudal part of the axilla, proceeding up towards the axillary vein and then continuing medially to the Berg level II. The long thoracic nerve and the thoracodorsal bundle should be identified and carefully separated from the axillary fat. The dissection may then follow the route of the thoracodorsal bundle to the axillary vein.

There is currently no consensus on the optimal handling of the intercostobrachial nerve(s) during AC [14–16, 18–20] and whether to preserve or perform a planned clean transection of the nerve(s) thus remains unclear. If the nerve(s) is cut, it should be performed sharply close to the thoracic wall medially and at the level of subcutaneous fat laterally.

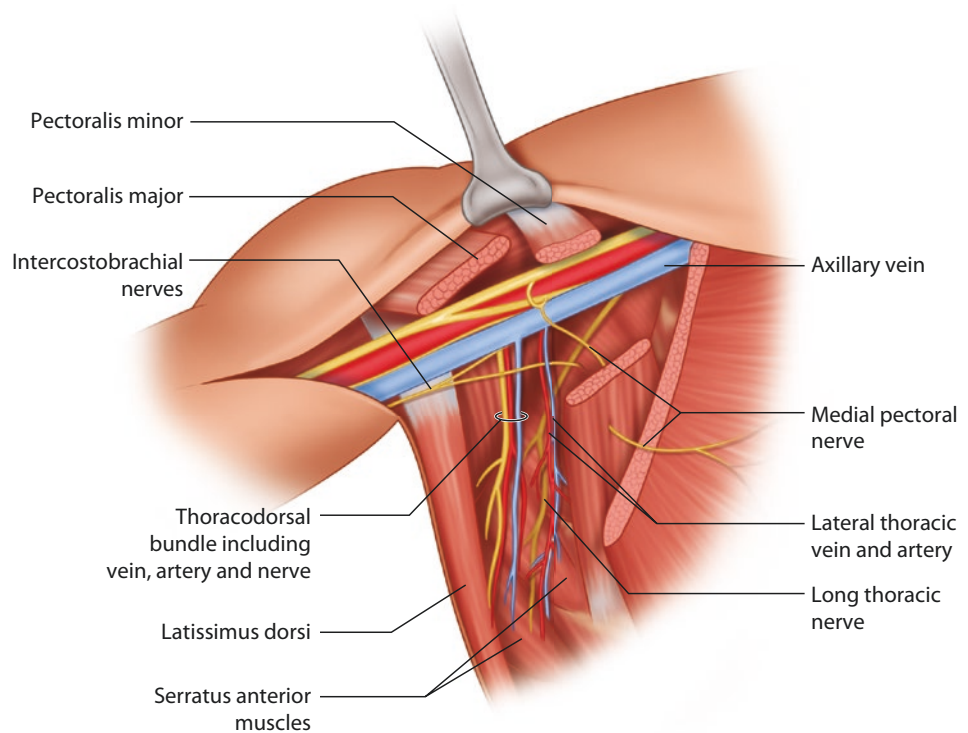
The AC is continued by dissection of the axillary fat from the lateral border of the pectoralis muscles, and the medial

pectoral pedicle is identified and preserved. The pectoralis muscles are then retracted anteriorly to facilitate the dissection of levels II and III by following the axillary vein medially. The lateral thoracic vein unites with the axillary vein at the border of levels I and II, and the lateral thoracic vessels may be spared if feasible. In special cases with challenging dissection of the level III nodes through the standard axillary approach, a direct transpectoral approach may be considered. In this approach the pectoralis major muscle is split anteriorly, and the pectoralis minor is retracted laterally, with the level III axillary fat accessed directly from the anterior direction [21].

There is considerable individual variation in the axillary anatomy regarding the neurovascular structures [16, 20, 22]. The axillary arch or Langer's arch is perhaps the most important anatomical variation concerning the AC [23]. It is an aberrant muscular slip of varying dimension, which typically arises from the latissimus dorsi muscle, crosses the axilla anteriorly to the axillary fat and connects with the pectoralis muscles. The axillary arch may need to be divided in order to facilitate axillary clearance.

After the axillary clearance, a careful palpation of the entire axilla must be performed, and all remaining suspicious nodes should be removed. In particular the interpectoral space, i.e. the space between the pectoralis minor and major muscles, should be palpated, and palpable nodes should be removed. The space between the thoracodorsal bundle and the long thoracic nerve and especially the lateral aspect of the junction of the thoracodorsal vein and axillary vein are typical locations for retained lymph node metastasis and subsequent lymph node recurrences (Fig. 24.3).

Fig. 24.3 Key anatomical structures of the axilla



Finally, meticulous haemostasis is performed, and closed-suction drainage may be left in the axilla, but this is a controversial subject at present. Seroma formation is common after axillary clearance, and a number of studies have looked at measures to reduce seroma incidence. Surgical obliteration of the dead space by quilting sutures seems to reduce seroma incidence both in the axilla and in the mastectomy area [24–26]. A 2013 Cochrane systematic review and meta-analysis concluded that based on seven randomized trials, there is limited quality evidence that wound drainage reduces seroma formation and the number of postoperative seroma aspirations [27]. A subsequent randomized trial of 596 breast cancer patients contested this finding by concluding that drainage did not reduce symptomatic seroma formation or interventions to treat seromas after axillary clearance [28].

Chronic postoperative morbidity after axillary clearance is covered in later chapters on lymphoedema and chronic pain. In summary, possible complications during and after AC include intraoperative damage to the neurovascular structures, seroma formation, postoperative haematoma, sensory disturbances, acute and chronic pain and lymphoedema. All of these complications are more common after AC than SLNB.

24.5 Pathological Analysis

The apical node may be marked with a suture to orientate the specimen. The extent of nodal involvement, including the highest extent, may influence RT indications and extent. Indications for irradiation of a wider lymph node area, such as the supraclavicular area, differ considerably between cen-

tres, and heavy nodal involvement or level III involvement may influence adjuvant radiotherapy field planning. At least ten lymph nodes should be found and examined in the pathology analysis of the axillary clearance specimen [29]. An increasing number of examined lymph nodes also increase the number of metastatic lymph nodes found and subsequently improve the accuracy of pathologic nodal staging [30].

Key Points

- Axillary clearance is used in staging the axilla only when sentinel lymph node biopsy is contraindicated.
- Axillary clearance is currently the standard of care in clinically node-positive patients.
- There is considerable variation in treatment algorithms regarding axillary clearance after metastatic sentinel lymph node finding.
- When axillary clearance is indicated, a routine dissection of Berg levels I and II should be performed.
- Axillary clearance aims at removing all cancerous tissue from the axilla.
- Key anatomical structures including the long thoracic nerve, thoracodorsal pedicle and medial pectoral pedicle need to be identified and preserved during axillary clearance.
- Complications, including seroma formation, chronic pain, sensory disturbances and lymphoedema, are more common after axillary clearance than sentinel lymph node biopsy.

References

- Fisher B, Redmond C, Fisher ER, Bauer M, Wolmark N, Wickerham DL, et al. Ten-year results of a randomized clinical trial comparing radical mastectomy and total mastectomy with or without radiation. *N Engl J Med.* 1985;312(11):674–81.
- Orr RK. The impact of prophylactic axillary node dissection on breast cancer survival—a Bayesian meta-analysis. *Ann Surg Oncol.* 1999;6(1):109–16.
- Heuts E, van der Ent F, van der Pol H, von Meyenfeldt M, Voogd A. Additional tracer injection to improve the technical success rate of lymphoscintigraphy for sentinel node biopsy in breast cancer. *Ann Surg Oncol.* 2009;16(5):1156–63.
- Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. *Lancet Oncol.* 2013;14(7):609–18.
- Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol.* 2014;32(13):1365–83.
- Giammarile F, Alazraki N, Aarsvold JN, Audisio RA, Glass E, Grant SF, et al. The EANM and SNMMI practice guideline for lymphoscintigraphy and sentinel node localization in breast cancer. *Eur J Nucl Med Mol Imaging.* 2013;40(12):1932–47.
- 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.
- Bundred NJ, Barnes NL, Rutgers E, Donker M. Is axillary lymph node clearance required in node-positive breast cancer? *Nat Rev Clin Oncol.* 2015;12(1):55–61.
- Galimberti V, Cole BF, Zurrada S, Viale G, Luini A, Veronesi P, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. *Lancet Oncol.* 2013;14(4):297–305.
- Van Zee K, Manasseh D, Bevilacqua J, Boolbol S, Fey J, Tan L, et al. A nomogram for predicting the likelihood of additional nodal metastases in breast cancer patients with a positive sentinel node biopsy. *Ann Surg Oncol.* 2003;10(10):1140–51.
- Meretoja TJ, Leidenius MH, Heikkilä PS, Boross G, Sejben I, Regitnig P, et al. International multicenter tool to predict the risk of nonsentinel node metastases in breast cancer. *J Natl Cancer Inst.* 2012;104(24):1888–96.
- Meretoja TJ, Audisio RA, Heikkilä PS, Bori R, Sejben I, Regitnig P, et al. International multicenter tool to predict the risk of four or more tumor-positive axillary lymph nodes in breast cancer patients with sentinel node macrometastases. *Breast Cancer Res Treat.* 2013;138(3):817–27.
- Berg JW. The significance of axillary node levels in the study of breast carcinoma. *Cancer.* 1955;8(4):776–8.
- Warrier S, Hwang S, Koh CE, Shepherd H, Mak C, Carmalt H, et al. Preservation or division of the intercostobrachial nerve in axillary dissection for breast cancer: meta-analysis of randomised controlled trials. *Breast.* 2014;23(4):310–6.
- Andersen KG, Aasvang EK, Kroman N, Kehlet H. Intercostobrachial nerve handling and pain after axillary lymph node dissection for breast cancer. *Acta Anaesthesiol Scand.* 2014;58(10):1240–8.
- Soares EW. Anatomical variations of the axilla. Springerplus. 2014;3:306.
- Nadkarni MS, Raina S, Badwe RA. Medial pectoral pedicle: a critical landmark in axillary dissection. *ANZ J Surg.* 2006;76(7):652–4.
- Andersen KG, Durlaud HM, Jensen HE, Kroman N, Kehlet H. Predictive factors for the development of persistent pain after breast cancer surgery. *Pain.* 2015;156(12):2413–22.
- Bruce J, Thornton AJ, Powell R, Johnston M, Wells M, Heys SD, et al. Psychological, surgical, and sociodemographic predictors of pain outcomes after breast cancer surgery: a population-based cohort study. *Pain.* 2014;155(2):232–43.
- Zhu JJ, Liu XF, Zhang PL, Yang JZ, Wang J, Qin Y, et al. Anatomical information for intercostobrachial nerve preservation in axillary lymph node dissection for breast cancer. *Genet Mol Res.* 2014;13(4):9315–23.
- Hadjiminas DJ, Zacharioudakis KE. Direct transpectoral approach for level III axillary lymph node clearance. *Ann R Coll Surg Engl.* 2014;96(6):481–2.
- Aripin YM, Ibrahim N, Muhammad R. Medial pectoral pedicle is a reliable landmark for axillary lymph node dissection. *Asian J Surg.* 2013;36(4):150–3.
- Jelev L, Georgiev GP, Surchev L. Axillary arch in human: common morphology and variety. Definition of "clinical" axillary arch and its classification. *Ann Anat Anat Anz Off Organ Anat Ges.* 2007;189(5):473–81.
- ten Wolde B, van den Wildenberg FJ, Keemers-Gels ME, Polat F, Strobbe LJ. Quilting prevents seroma formation following breast cancer surgery: closing the dead space by quilting prevents seroma following axillary lymph node dissection and mastectomy. *Ann Surg Oncol.* 2014;21(3):802–7.
- Ouldamer L, Bonastre J, Brunet-Houdard S, Body G, Giraudeau B, Caille A. Dead space closure with quilting suture versus conventional closure with drainage for the prevention of seroma after mastectomy for breast cancer (QUISERMAS): protocol for a multicentre randomised controlled trial. *BMJ Open.* 2016;6(4):e009903.
- Kottayasamy Seenivasagam R, Gupta V, Singh G. Prevention of seroma formation after axillary dissection—a comparative randomized clinical trial of three methods. *Breast J.* 2013;19(5):478–84.
- Thomson DR, Sadideen H, Furniss D. Wound drainage after axillary dissection for carcinoma of the breast. *Cochrane Database Syst Rev.* 2013;10:CD006823.
- Taylor JC, Rai S, Hoar F, Brown H, Vishwanath L. Breast cancer surgery without suction drainage: the impact of adopting a 'no drains' policy on symptomatic seroma formation rates. *Eur J Surg Oncol.* 2013;39(4):334–8.
- Del Turco MR, Ponti A, Bick U, Biganzoli L, Cserni G, Cutuli B, et al. Quality indicators in breast cancer care. *Eur J Cancer.* 2010;46(13):2344–56.
- Schaapveld M, de Vries EG, van der Graaf WT, Otter R, de Vries J, Willemse PH. The prognostic effect of the number of histologically examined axillary lymph nodes in breast cancer: stage migration or age association? *Ann Surg Oncol.* 2006;13(4):465–74.