

A systematic review of the complications of skin puncturing procedures in the upper limbs of patients that have undergone procedures on the axilla or breast

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Background: The increasing incidence and prevalence of breast malignancies have led to increasing numbers of surgical interventions performed on the axilla and breast, including axillary lymph node dissection (ALND), sentinel lymph node biopsy (SLNB), and mastectomy. The risk of postoperative complications, like breast cancer-related lymphoedema (BCRL), can have significant deleterious cosmetic and quality of life effects. National guidelines and cancer councils publish recommendations to avoid skin puncturing procedures, such as venepuncture and intravenous (IV) cannulation, on arms ipsilateral to the surgical site to prevent BCRL occurrence. The initial trials that established a link between BCRL and skin puncture were conducted in the 1950s and 1960s; the evolution of surgical management of breast cancer has likely led to large decreases in complication rates.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, four databases were systematically searched for relevant articles. Eleven relevant articles were identified for inclusion in the final analysis. Updated Australian and New Zealand College of Anaesthetists & Faculty of Pain Medicine (ANZCA) guidelines were included in the analysis following their publication after the initial search had been completed.

Results: The overall quality and quantity of evidence in this field is sufficient to conclude that skin puncturing procedures on ipsilateral arms should not be avoided in patients with previous breast or axillary surgery. The highest-quality and most recent available evidence does not support an association between BCRL and skin puncturing procedures. Policies and practices that advocate avoiding skin puncture procedures to prevent BCRL may lead to delays in clinical care. The 2023 ANZCA guidelines recommend against avoiding affected arms for peripheral access and suggest the removal of institutional policies preventing this practice.

Conclusions: In patients that have undergone breast surgery or axillary procedures, venous access procedures can be safely performed on the ipsilateral arm. The evidence does not support overarching restrictions on using the ipsilateral arm without pre-existing lymphoedema.

Keywords: Lymphedema; breast cancer; axillary lymph node dissection (ALND); sentinel lymph node biopsy (SLNB); intravenous cannulation (IVC)

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Introduction

Background

Breast cancer is a disease with high incidence and prevalence, requiring large volumes of surgical interventions for its management. The current standard of care for primary breast malignancies includes treatment with chemotherapy, mastectomy or segmental mastectomy, and sentinel lymph node biopsy (SLNB). Radiotherapy (RT) and chemotherapy are adjuvant therapies that are sometimes used for breast cancer treatment at the discretion of the treating team. Axillary lymph node dissection (ALND) may be used as a treatment strategy for locally-advanced malignancies. These procedures are associated with inherent risks of systemic and local tissue damage risks, particularly in the anatomical areas targeted by segmental mastectomy, SLNB, ALND, and RT. A common adverse effect of breast cancer therapy is lymphoedema of the affected side, with a reported prevalence of 20–49% (1-4). Lymphoedema is characterised by swelling and deformity of the upper extremity, resulting in loss of function and significant limitation of motion. Preventing breast cancer-related lymphoedema (BCRL) is critical for patients' quality of life, as it is a permanent

condition that can be severely disabling (4). BCRL is a clinical diagnosis with no diagnostic biomarkers or concrete evidence used for diagnosis other than the circumference of the affected limb (5). Therefore, different centres and studies have used a wide range of diagnostic cutoffs for BCRL, resulting in a lack of standardisation when comparing clinical data.

Among risk factors identified in the development of BCRL, one of the strongest associations is injury or infection of the affected limb (1-4,6). Therefore, a key measure for reducing lymphoedema incidence is preventing damage to the limb. Medical treatment team members often attempt to prevent damage to limbs by avoiding procedures that may cause injury to the limb. These beliefs are also commonly held by patients themselves. In a 200-patient survey conducted in Canadian oncology centres, 75% of patients reported believing that blood draws and blood pressure measurements on their affected arm would increase their risk of developing lymphoedema (3). Major associations, including the American Cancer Society, also advise patients to advocate for avoiding procedures on their affected arms (7). This has led to modifications in clinical practices, including intravenous access and venepuncture (8). A common clinical practice is avoiding using an upper limb that has undergone an ipsilateral segmental mastectomy, RT, SLNB, or ALND to obtain intravenous (IV) access or blood samples (6,9). Historically, hospital policies and clinicians have perpetuated the perceived association between IV access and the risk of lymphoedema development (9). However, these beliefs have not been supported by a large base of scientific evidence. Additionally, the logistical constraints imposed upon clinicians by these policies can potentially negatively affect the provision of appropriate care.

Highlight box

Key findings

- Recent high-quality research indicates no association between ipsilateral cannulation on arms and previous axillary lymph node dissection, sentinel lymph node biopsy, and mastectomy with breast cancer-related lymphoedema (BCRL).
- Professional guidelines have been updated accordingly.

What is known and what is new?

- Earlier studies suggested a potential link between ipsilateral cannulation and BCRL risk.
- Limited large-scale studies explored this connection until recently.
- Recent studies (Yanagita et al. and Naranjo et al.) found no significant differences in BCRL outcomes between ipsilateral and contralateral cannulation in patients with surgical breast cancer treatments.
- 2023 Australian and New Zealand College of Anaesthetists & Faculty of Pain Medicine guidelines recommend against avoiding ipsilateral cannulation in these patients.

What is the implication, and what should change now?

- Avoiding ipsilateral cannulation unnecessarily impacts clinical care efficiency.
- Considering the lack of evidence indicating BCRL risk, modify clinical policies that discourage this practice.

Rationale and knowledge gap

Policies that prevent clinicians from ipsilateral arm cannulation are cumbersome due to the universal use of IV access devices in clinical settings. Intravenous cannulation (IVC) is a ubiquitous clinical procedure that is used to deliver medications or fluids to the bloodstream for treatment. Although IVC is a routine procedure, it is nevertheless associated with intrinsic risks, including mechanical damage to the skin and venous tissue. Complications of IVCs include thrombophlebitis and, in rare cases, bacteraemia and septicaemia (6,10,11). On the other hand, IVC placement is cost and time effective, especially within inpatient settings. Administration of

IV fluids, antibiotics, and other IV medications is most commonly achieved through a peripheral IVC. The currently accepted clinical practice of avoiding the arms of patients undergoing breast cancer treatment on that side may impede the timely and effective delivery of IV medications, especially in scenarios where multiple IVCs must be placed simultaneously. To balance the provision of appropriate IV access to patients that have undergone breast cancer treatment with the risk of developing complications, this review aims to establish the current level of evidence for the practice of avoiding peripheral IVC placement in affected arms.

Other literature reviews have been conducted to answer this question, with the most recent being done in 2014 (12) and 2015 (13). The authors of both studies concluded that while there is a paucity of high-quality evidence that can be used to answer the research question, the research that does exist in the literature supports the conclusion that ipsilateral arm cannulation following surgical procedures does not increase the risk of lymphoedema development. This review aims to add to the literature by examining developments within the past decade that can more conclusively ascertain the validity of the current clinical practice.

Objective

This systematic review aims to provide an overview of the current evidence available in the literature for avoiding IVC placement in the upper limbs of patients that have had procedures on the axilla or the breast. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework for systematic reviews, relevant articles in the literature were identified and analysed to answer the research question (14). We present this article in accordance with the PRISMA reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-23-1400/rc>).

Methods

Eligibility criteria

Prior to database searching, eligibility criteria for inclusion in the review were established. The publication date was restricted to within the last 30 years at the time of the review [1992–2022]. Only English-language publications were considered eligible. All study designs and settings examining the following interventions were considered

eligible: breast surgery, axillary surgery including SLNB and axillary lymph node clearance, axillary RT, chest wall RT, and pre-existing upper limb lymphoedema. The primary outcome of interest in this review was BCRL, but other complications associated with cannulation such as thrombophlebitis and infections were considered eligible. Formal studies were included; letters, editorials, and non-systematic literature reviews were excluded.

Information sources

Searches were conducted on multiple databases, including OVID Medline, Cochrane Reviews, EMBASE, and Scopus. The review registry PROSPERO was searched for similar systematic reviews. Bibliographies of articles returned in the primary search were manually screened for relevant studies to be included in the final analysis. No experts or authors of unpublished literature were consulted. Database searches were conducted in June 2022.

Search strategy

A list of MeSH keywords was pre-determined before commencing the search. The keywords were inputted into the advanced search forms of the databases using specific combinations and modifiers. See [Appendix 1](#) for full MeSH term list.

The search returned 179 results from the databases listed above, which were combined, screened for duplicates, and assessed for relevance to the research question. Items were excluded if they did not include the target population, intervention, or outcome. The bibliographies of relevant items included after primary screening were also manually screened for relevant articles, which were subsequently included in the total screening count. Following the initial search and screening process, the Australian and New Zealand College of Anaesthetists (ANZCA) released a guideline update in 2023 pertaining to peripheral venous access in patients with previous ALND. These guidelines were included in the analysis. Please refer to [Figure 1](#).

Selection process

Two independent reviewers screened returned search items on Rayyan.ai. Relevant results were included in the study based on their target population, intervention, methodology, and validity. There were no disagreements between the independent reviewers concerning study

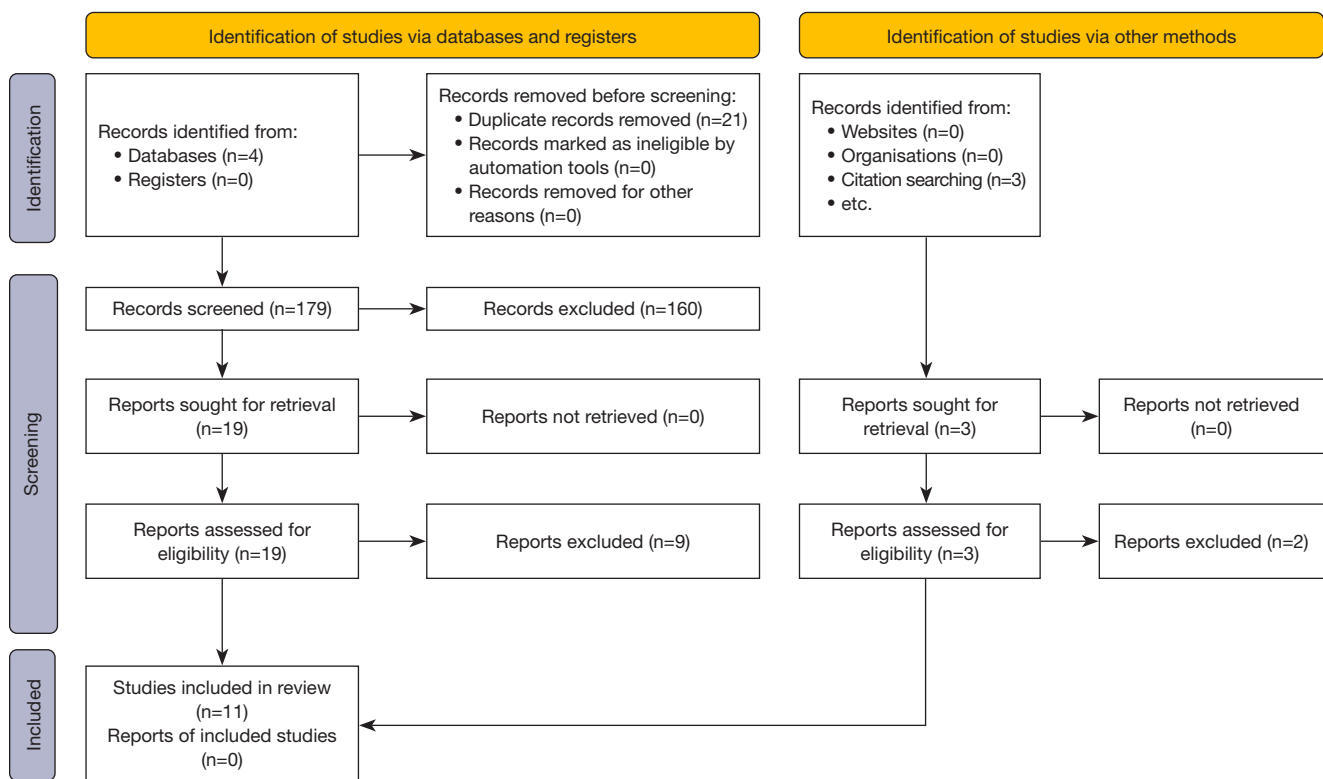


Figure 1 PRISMA flow diagram illustrating the review process.

inclusion. Following duplicate removal and screening, 11 studies were included in the final analysis. The most recent ANZCA guidelines were published after completion of the analysis and are further discussed below.

Data collection process

Two independent reviewers collected data manually upon review of the items included in the analysis.

Study risk of bias assessment

Efforts to minimise bias included searching multiple databases, using two independent reviewers during the screening process and excluding editorials and opinion articles from the dataset. The manual screening of bibliographies of included items could have introduced reviewer bias in article selection.

Synthesis methods

The disparate study designs of included articles and the

paucity of high-quality study designs in the literature led to a narrative-driven synthesis of information in the analysis.

Results

Study selection

Eleven studies were included in the final analysis. These articles represent the highest-quality evidence returned from the search. Please refer to *Table 1*.

Discussion

The high prevalence and incidence of breast cancer, combined with advances in surgical therapies for breast cancer, have resulted in a large population at risk of BCRL (1-4,6). Patients who have undergone procedures on the axilla and breast are understandably proactive in taking measures to limit their risk of developing lymphoedema, including ipsilateral cannulation (3). Before the past decade, the state of the evidence regarding the association between ipsilateral cannulation and BCRL was severely limited, and

Table 1 Study characteristics based on the level evidence matched with NHMRC guidelines (15)

Study title	Level of evidence (NHMRC) (15)	Study design	Study population	Total N	Outcome
Naranjo <i>et al.</i> , 2021 (16)	III-2	Retrospective cohort	Patients post-breast cancer surgery +/- ALND	7,896 intravenous placements in 3,724 patients	No significant difference in BCRL development between ipsilateral and contralateral cannulation
Asdourian <i>et al.</i> , 2016 (17)	I	Literature review	31 studies	10 studies examining skin puncture	2/10 studies found increased risk of BCRL with skin puncture
Yanagita <i>et al.</i> , 2014 (18)	II	Multicentre RCT	Patients with ALND + adjuvant chemotherapy + no lymphoedema at enrolment	44: 22 controls excluded from ipsilateral cannulation, 22 in experimental group	No significant difference in BCRL between groups; control group had increased risk of phlebitis
Higton <i>et al.</i> , 2011 (19)	I	Literature review	8 studies examining skin puncture and lymphoedema	8 studies	1 study (Clark 2005) found increased risk of BCRL post-skin puncture, 7 found no increased risk
Smith, 1998 (20)	IV	Case series	Patients with ALND +/- radiotherapy with lymphoedema	10	Anecdotal evidence of association between ipsilateral venepuncture and BCRL
Jakes & Twelves, 2015 (13)	I	Literature review	7 studies	7 studies	Paucity of evidence to demonstrate harm from ipsilateral cannulation
Clark, 2005 (21)	II	Prospective cohort	Patients post ALND or SLNB, with no advanced disease	251, with 75% completing 3-year follow-up	Hospital skin puncture associated with 2.44 RR of BCRL development
Chan, 2009 (22)	III-2	Case control	Patients post unilateral ALND	202	OR of lymphoedema following ipsilateral skin puncture =0.57 (95% CI: 0.31–1.12)
Cheng <i>et al.</i> , 2014 (12)	I	Literature review	3 studies	3 studies	No convincing evidence of association between skin puncture and BCRL
Hayes <i>et al.</i> , 2005 (23)	IV	Cross-sectional study	Patients with unilateral breast cancer younger than 75 diagnosed within the last 6 months	176	Ipsilateral blood pressure measurement increased BCRL risk, no association between BCRL and skin puncture
Levasseur <i>et al.</i> , 2018 (9)	IV	Cross-sectional study	Survey of oncology physicians and nurses	25 physicians and 57 oncology nurses	ALND and SLNB were the factors most perceived by physicians and nurses to increase BCRL risk. 12% of physicians and 33% of nurses reported blood tests as perceived risk factors for BCRL development

NHMRC, National Health and Medical Research Council; ALND, axillary lymph node dissection; BCRL, breast-cancer related lymphedema; RCT, randomized controlled trial; SLNB, sentinel lymph node biopsy; RR, risk ratio; OR, odds ratio; CI, confidence interval.

mainly consisted of case reports and small-scale studies. Additionally, some current guidelines cautioning against ipsilateral skin puncture post-surgery were derived from studies performed in the 1950s and 1960s, before the advent of modern breast surgery (24,25). Nevertheless, the belief that ipsilateral cannulation can result in lymphoedema has persisted in both the practice of healthcare professionals and in patients' beliefs. Additionally, the Breast Cancer Network of Australia recommends avoiding skin puncture of ipsilateral arms following breast cancer surgery, whilst acknowledging the lack of evidence to make that recommendation.

Studies conducted in the early 2000s presented conflicting evidence regarding the development of BCRL following ipsilateral cannulation. The 2005 Clark *et al.* study recruited 251 patients who had undergone ALND, lymph node biopsy, or sampling and followed them for 3 years post-procedure (21). With 75% completion of follow-up, the authors found an RR of 2.4 for developing BCRL with ipsilateral cannulation instead of avoiding ipsilateral skin puncture. On the other hand, another similar study by Chan was conducted in 2009 (22). This case-control study matched patients with lymphoedema with controls without lymphoedema; patients in each group had previously undergone unilateral ALND. The authors found a decreased odds ratio (OR) of BCRL development in patients undergoing ipsilateral skin puncture [OR =0.57, 95% confidence interval (CI): 0.31–1.12]. The contrasting outcomes of these small-scale studies indicated a need for larger and better-powered studies for establishing a link between IV cannulation and BCRL risk.

The uncertainty of available evidence at the time was a common theme in the literature reviews. Authors of all reviews were unanimous in the paucity of evidence in the field and were unable to form strong evidence-based recommendations. The conflicting findings of the studies published in the 2000s led to the authors calling for more robust study designs with larger sample sizes to demonstrate a harm association conclusively. The Jakes & Twelves review from 2015 was cited as supporting evidence in the updated ANZCA guidelines that recommend against avoiding ipsilateral skin puncturing procedures (13).

The Yanagita *et al.* study from 2014 and the Naranjo *et al.* study from 2021 highlight the most recent developments in the evidence base for making recommendations regarding ipsilateral cannulation (16,18). The Yanagita trial was a multicentre RCT with 44 participants that had previously undergone ALND and adjuvant chemotherapy. The participants were separated into a control group,

in which patients did not receive ipsilateral cannulation, and an experimental group, where ipsilateral cannulation was performed alternately with vascular access on the contralateral arm. Development of BCRL was defined as enlargement of the arm, elbow, wrist, or hand by 2 cm or more compared to the contralateral upper extremity. Four patients in each group developed lymphoedema (18%, 95% CI: 5.2–40.3%). Although there was no significant difference in the development of BCRL, the control group experienced more phlebitis (27% *vs.* 14%). The higher rate of phlebitis in the control group highlights the risks of excluding potential cannulation sites on ipsilateral arms, such as “overuse” of veins resulting in clinically significant complications. This trial was limited by the small sample size and short trial period (3 weeks). Although the quality of the evidence provided by this trial is low, it signals a lack of harm caused by ipsilateral cannulation.

The recent Naranjo *et al.* study from 2021 is likely the highest-quality available trial examining this research question (16). It should be a cornerstone of any recommendation concerning ipsilateral cannulation post-surgery. This was a retrospective cohort study conducted by chart review of patients with a history of breast cancer surgery that had received IV cannulas between January 1, 2015, and May 5, 2018. The study included 3,724 patients that had received a total of 7,896 IV cannulas. Of 2,743 contralateral IVs, 2 had a complication, while out of 5,153 ipsilateral IVs, 2 had a complication. There was no significant difference in complication rates between the groups ($P=0.91$). Both complications identified in the ipsilateral IV group occurred years after the patients' breast surgeries and were characterised by spontaneously resolving lymphoedema that did not require long-term treatment. In both cases, the lymphoedema could possibly be attributed to factors other than their surgical histories, such as complex medical comorbidities. In the context of the very low complication rates experienced by either group, or the lack of difference between the groups, the authors concluded that avoiding cannulation in arms ipsilateral to prior breast surgery is an unnecessary clinical practice. Although this study was inherently prone to bias due to its retrospective design and reliance on electronic medical record (EMR) data, it nonetheless represents the best powered and most well-designed study intended to address the research question. Another limitation of this study is insufficient long-term follow-up data due to a lack of EMR records following hospital discharge. This may have contributed to under-reporting of delayed IV-

related complications that occurred in the community. A significant confounding factor mentioned by the authors is the pervasive patient-facing messaging from institutions advocating against ipsilateral cannulation, which could have led to more patient-driven refusals of ipsilateral cannulation in higher-risk patients.

The updated ANZCA guidelines from 2023 indicate a shift in professional guidance regarding IV cannulation in patients with previous ALND (26). Negative patient and institutional views of IV cannulation in affected arms have been implicated in the impedance of anaesthetic care (27). These guidelines state that the overall evidence for avoiding ipsilateral cannulation of affected arms is poor, except for when significant lymphoedema is already present in the affected arm. The risks of alternative access, such as central venous access, are likely to outweigh the benefits of avoiding IV access in affected arms. The guidelines recommend the removal of institutional policies that restrict peripheral venous access in affected arms with ALND. Additionally, the guidelines state that there is “no contraindication” to IV cannulation of the affected arm. The risks of avoiding peripheral access in affected arms include overuse of veins in contralateral arms, patient discomfort from using lower limb access sites, and the inherent risks associated with central venous access. A potential limitation of this guideline includes the context for which it is intended; peripheral cannulae for anaesthetic delivery and monitoring are typically left in-situ for shorter periods of time than cannulae used in other clinical settings.

On the weight of recent developments within the field and changes in official policies by professional bodies such as ANZCA, it is unlikely that ipsilateral cannulation post-breast surgery increases the risk of BCRL development.

Limitations

An issue faced by evidence concerning this research question is the inability to carry out blinded RCTs due to the nature of the intervention. Therefore, the highest quality extant evidence comes from relatively small-scale observational and cohort studies. The Naranjo trial currently represents the highest quality evidence available in the field. Updated expert guidelines have also noted the absence of high-quality evidence that can be used to fully answer the research question. Although further large-scale studies would be warranted to answer the question, it is unlikely that they will be cost- and time-effective considering the negative results of more recent trials.

Other limitations include a lack of standardisation of BCRL diagnosis and the use of different diagnostic cut-offs to determine whether or not a limb is affected by lymphoedema. The lack of diagnostic standardisation is a key hindrance in comparing different trials that may have used different criteria in arriving at a BCRL diagnosis. Lastly, when designing trials investigating the impact of skin puncture, it is difficult to control for other factors that are more likely to predispose patients to BCRL, such as obesity, infection, and trauma.

Conclusions

The current “level of evidence” for avoiding ipsilateral skin puncture procedures on arms that have undergone previous surgical procedures is poor overall. The highest-quality and most recent evidence does not demonstrate a relationship between skin puncture and BCRL development. Recently communicated position statements from ANZCA have stated that there is “no contraindication” to ipsilateral skin puncturing procedures and have recommended that institutions revise official protocols to reflect this. Based on the literature available at the time of this review, the authors do not recommend avoiding these procedures, especially if they impede clinical care delivery.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://atm.amegroups.com/article/view/10.21037/atm-23-1400/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Appendix 1 MeSH term list

1. Administration, Intravenous
2. Venipuncture
3. Axilla
4. Breast
5. Mastectomy, Segmental
6. Mastectomy
7. Surgical Procedures, Operative
8. Sentinel Lymph Node Biopsy
9. Radiotherapy, Adjuvant
10. Radiotherapy
11. Thoracic Wall
12. Lymphedema
13. Breast Cancer Lymphedema
14. Postoperative Complications
15. Infusions, Parenteral
16. Blood Specimen Collection
17. Limb precautions