

MORE ON AXILLARY LYMPHADENECTOMY

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“Trivia make perfection,
but perfection is not trivial”
— Michelangelo

A previous Editorial (1) and a Letter to the Editor (2) addressed axillary nodal dissection and secondary lymphedema of the arm. Lymphedema of the arm is perhaps the greatest disability a woman has to face after standard treatment for breast cancer (modified radical mastectomy or “lumpectomy,” axillary nodal sampling with regional irradiation) (3-6). Not surprisingly, a patient with breast cancer without arm lymphedema copes much better with cancer-related psychological issues (7). Difficulties with a “fat arm,” daily problems with clothing, positioning the arm at rest, interpersonal relationships, occupational aspirations, and self-esteem are all a consequence of arm lymphedema.

According to the American Cancer Society, over 180,000 women in the USA develop breast cancer annually (8) with the incidence of secondary arm lymphedema varying from 2.7 to 72% (9-12). The incidence of this complication has not changed after partial mastectomy, lumpectomy, irradiation, and modified radical mastectomy (13).

Why do not all patients develop a swollen arm after axillary nodal dissection?

Halsted in 1921 and later others (5) concluded from clinical experience and laboratory research that the mere localized interruption of lymph flow in the axilla does not uniformly result in secondary arm

lymphedema, which is supported by the aforementioned wide incidence of its occurrence.

To investigate the various factors (lymphatic-lymphatic anastomoses, collateral lymphatic circulation, lymphatic-venous anastomoses, macrophage protein digestion), various animal experimental counterparts for secondary limb lymphedema were produced. In this context, the enormous regenerative potential of lymphatic vessels was described by Gray, “Severed lymph-collectors can unite by sprouting, which is the growth of narrow thin walled lymphatic vessels from the stumps of severed cells. These establish connections with stumps of lymph collectors on the other side of the wound. First, there are solid endothelial protrusions from preexisting lymphatic endothelium which then develop a lumen” (14).

In humans, “lymphatic wound repair” takes no longer than 7 days (15). Gray (14) also adds “remodeling and elaboration of preexisting small vessels into large definitive trunks occurs in response to altered conditions.”

QUALITY OF AXILLARY DISSECTION

An exact analysis of 1155 patients with axillary dissection and secondary arm lymphedema was carried out by Gregl (10). The surgical factor: uncomplicated healing of the axilla was present in only 22%. The incidence of secondary arm lymphedema varied widely (5,6,8-12), raising the specter



Fig. 1. A “horrible” axillary dissection line directly interrupting arm lymphatics. Left axillary incision for lymphadenectomy, extending (a “don’t”) into the upper arm.

that the quality of axillary dissection and of post-operative care were critical issues in the development of secondary arm lymphedema. I believe that uncomplicated wound healing and absence of both local tumor recurrence and secondary arm lymphedema are expected by the patient as evidence of optimal surgical training and know how. Quality of therapy reduces open and hidden costs (16,17). Does the skill of the operator and of one’s techniques in performing a radical axillary dissection influence subsequent arm lymphedema? To this question the author has no exact statistical answer (18). Winiwarter (19) writes: “The results, using the same method, but by different physicians, differ greatly.” For example, a study of long-time outcomes of surgical therapy for 1157 solitary colo-rectal cancer patients (20) reveals the surgeon to be a specific prognostic factor. Further statistical analysis (21) concerning 1000 surgical outpatient procedures also reveals differences in incidence of wound dehiscence, tissue reactivity and infection, related to the surgeon’s skill.

AXILLARY DISSECTION – WHAT TO DO WITH TRANSECTED LYMPHATICS?

Direct operative injury to draining lymphatics from the arm should be avoided (*Fig. 1*). After opening the axilla for dissection, the abducted arm is rotated externally. It has been stated that ligation of lymphatics is unnecessary since external drainage to the axillary fossa is effective in preventing a lymphocele (2). Lymph, an ultrafiltrate of blood plasma, contains in general less protein than plasma, and the lowest protein concentration is found in extremity lymph (22). These same authors (22) found clotting factors in lymph to be lower than 50% of plasma and, correspondingly, a prolonged clotting time. Similar findings were later observed in lymph collected during operations for lymphedema, both in the experimental animal and in humans (5). After axillary dissection, shoulder immobilization without direct compression towards the “axillary pyramid” (*Fig. 2*) was performed to avoid fluid leakage from the axilla, which proved vexing and cumbersome for the patient.

Accordingly, with the aid of loupe magnification, the axillary tissues to be dissected are severed between short-term absorbable ligatures. The pressure exerted

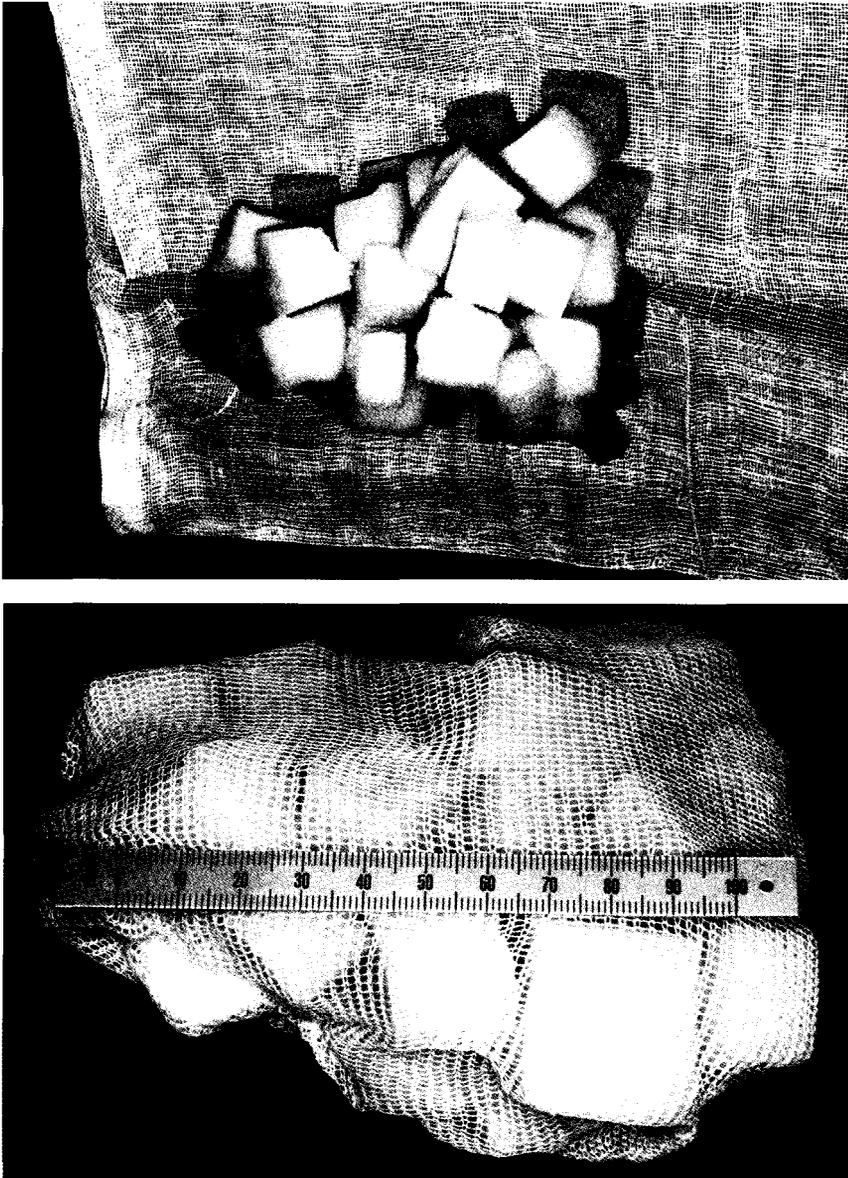


Fig. 2. Post axillary lymphadenectomy compression: (upper) Foam rubber cubes forming a pyramid, to be (lower) covered by gauze and pushing the closed skin incision towards the apex of the nodectomized axilla.

(Fig. 2) prevents hematoma and lymphocele formation — the lymphatics being a low pressure system. No electrocoagulation is used and minimal tissue damage is sustained to allow lymphatic-lymphatic anastomoses to occur. Ligation is considered a compromise between no injury to the axillary wound pyramid and the exerted intralymphatic

low pressure, thereby preventing a fluid collection and allowing for early removal of the axillary drains.

INFECTION

Lymph in the axilla may be seeded or contaminated by bacteria, viruses, and fungi



Fig. 3. Conventional lymphography demonstrating lymphatics within the sheath of the axillary vein.

(2) but seeding does not necessarily mean clinical infection. Many humans may inhale tubercle bacilli but only a small number will get clinical tuberculosis. On the other hand, if susceptible, humans infected with smallpox virus almost all will clinically fall ill. Overt infection needs a "suitable" medium, "dead space," and "fluid accumulation," which in the case of axillary dissection must be prevented.

SECONDARY ARM LYMPHEDEMA AND THE AXILLARY VEIN

Ligation of the axillary vein in the

human does not lead to phleboedema or lymphedema (5). Performing lymphatic-venous shunts in unaltered extremities does not induce lymphedema. *Fig. 3* demonstrates contrast medium injected into the lymphatics of the arm which lie within the perivascular tissues surrounding the axillary vein. In the individual breast cancer patient, I never skeletonize the axillary vein. Is this acceptable from an oncologic standpoint? I have never seen tumor or tumor recurrence in the tissues around the axillary vein, at or following axillary dissection, and I am unaware of references concerning this aspect.

"Restricted venous drainage ... aggravating arm edema" (2): In a recent paper, Stanton et al (23) found no significant hemodynamic contribution to postmastectomy lymphedema. However, in existing lymphedematous arms, alterations of blood vascularity resulted in secondary tissue changes (24-26).

What are the known mechanisms for wound healing including vessel reformation? Wound repair, still understood only partly, is highly complex. Cellular processes are regulated by growth factors and cytokines, some with overlapping functions (27). An example is the complicated system of macrophages which can be stimulated (28) and are involved in angiogenesis with Tie receptors and vascular endothelial growth factor (VEGF). In vasculogenesis, endothelial precursor cells [even described by Gray (14)] termed angioblasts, form and differentiate into endothelial cells, which form a primitive vascular plexus that in turn differentiates into various types of vessels, a process termed angiogenesis. Factors involved are multiple, such as VEGFs and their receptors, angiopoietins 1 and 2 and their Tie receptors, and integrin alpha V beta 3. Which factors are best to enhance wound repair? Studies to determine the optimal combination of growth factors to be applied clinically, with necessary different receptors and target cell effect so far have not yet been well defined in humans (29). But the tenets of meticulous, atraumatic

surgical technique are still critical as we apply guided generation—or regeneration of tissue components (27). “Diffusion” of lymph into the axilla does not replace canalicular lymph transport.

In conclusion, whether to ligate or not ligate afferent lymphatics to the axilla for allowing the complex formation of lymphatic-lymphatic communications is probably of minor importance. However, even small axillary fluid collections between tissue compartments that lead to scar formation (and both quantitative and qualitative reduction of newly formed lymphatics) (30) and prolonged suction catheter drainage are best avoided.

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Editor's Note

Although much of the meticulous dissection technique advocated by Clodius is to be admired, the status of axillary nodal dissection is currently undergoing a dramatic evolutionary change. Thus, many women with breast cancer over the age of 70 years are no longer being subjected to axillary nodal dissection but rather are simply placed on tamoxifen or an equivalent drug on the assumption that whether the nodes are positive or negative for metastasis, hormonal therapy is still the indicated treatment. Moreover, the introduction and now almost the standard care, namely sentinel node biopsy, has dramatically reduced the need for full axillary nodal dissection in most patients. Further, although controversial, many surgeons do not advocate axillary nodal

staging in patients with DCIS (ductal carcinoma in situ), the most common breast cancer picked up on screening mammography as the yield of metastatic disease with this "malignancy" in the axilla is so low. Finally, increasing recognition of breast cancer cells in bone marrow aspirate at time of presentation is raising the question of the value of staging nodal dissection as both hematogenous and lymphatic dissemination seem to be ongoing simultaneously. Perhaps staging axillary nodal dissection, though still popular, is destined to slowly disappear much as splenectomy and intraabdominal nodal sampling have disappeared for staging Hodgkin disease.

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