Side effects following conservative therapy for a carcinoma of the breast

Initial results with Hivamat (histological variable-manual technique)

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Conservative breast carcinoma therapy recommended at present only with postoperative irradiation - side effects entailed: fibroses, sensitivity disturbances, skin alterations, edema, restrictions of movement - Hivamat, due to improved flow equilibrium, largely prevents local edemas and pain - special form of manual lymph drainage - can be used postoperatively at once - own results good

Introduction

Conservative treatment, paying strict attention to the indications and contra-indications, occupies a firm place in today’s breast carcinoma therapy procedures. Numerous prospective and retrospective studies show that the overall rate of survival and the rate of recurrence-free survival for mastectomy patients and those patients submitting to conservative treatment are essentially identical, provided that similar tumor stages are compared (12, 16, 20, 22, 29, 33, 38, 39, 42).

The goal of conservative treatment is, in addition to permitting a reliable locoregional control, to produce an optimal cosmetic result with as few side effects as possible, as well as greatly reducing the physical and psychological stress to the patient, thus ensuring a high quality of life.

Conservative procedures are today generally combined operative-radiological therapies (6, 11, 12, 20, 36). It is precisely with these patients that Hivamat most clearly demonstrates its capabilities, because - along with the trauma of operation - the skin and also the remaining breast tissue become damaged in addition, due to postoperative interstitial and/or percutaneous radiation.

Until now, manual lymph drainage has been utilized in order to eliminate one of the consequences of an operation and/or irradiation, namely the lymphedema, as soon as it appears: in some cases as much as 1 to 2 years after treatment.

Our development of a special form of manual lymph drainage ("Hivamat") has made it possible to begin using this procedure prophylactically from the first day postoperative, in an attempt to prevent the formation of a lymphedema as can be expected at a later point in time, through a sufficiently early rechanneling of the lymph drainage paths. To our surprise, the technique has also proved to be successful in inhibiting the occurrence of other typical side effects usually incurred following treatment.
The present study presents initial results concerning the side effects following conservative therapy and optimization of therapy in regard to reducing side effects in those patients treated with Hivamat.

Patient population and method

At the gynecological clinic in Amburg, since November 1987, the side effects and psychic states observed during postoperative stationary tumor control and during special consulting hours devoted to the cosmetic aspects of surgery in patients having undergone a breast carcinoma operation were evaluated. All patients were assessed by the same physician, in most cases several times at intervals of 6 months.

Of particular importance to the study was the documentation of the following clinical criteria:

1. Consistency of operated and irradiated breast compared with other side
2. Pain, disturbances in sensitivity of the breast treated
3. Skin alterations (hypertanification, depigmentation, edema, erythrodema, telangiectases, desquamation, Iysis, necrosis, etc.)
4. Arm mobility and fine motor response
5. Pain, paresthesias, sensation of tenseness in the arm or axilla of the operated side
6. Lymphedema (as revealed by three-point measurement, compared with other side)

The Hivamat (histologically variable manual lymph drainage technique) intensification system decidedly enhances the effectiveness and lasting benefit of the known manual massage techniques.

Physical principle

A strong, pulsating electrostatic field is built up between the hands of the attending therapist and the body of the patient, which becomes effective during the massage. The hands determine the pressure applied to the tissue, controlling and defining the course of the procedure. A pervasive vibrational and pumping effect arises, penetrating deeply into the tissue. This greatly intensifies the effectiveness of classical massage techniques, as well as those of connective tissue massage and manual lymph drainage.

The maximum voltage applied is 500 Volts, while the current strength is in the microampere range. The maximum voltage source is a high internal resistance, controlled and defining the course of the procedure. A pervasive vibrational and pumping effect arises, penetrating deeply into the tissue. This greatly intensifies the effectiveness of classical massage techniques, as well as those of connective tissue massage and manual lymph drainage.

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The unit was developed by Zeidel and Waldner, specialists for massage treatment in the physical therapy department of the City of Amburg Marienkrankenhaus it has been used in surgery, urology, pediatrics, internal medicine, ENT and gynecology, as well as for the entire outpatient postoperative control examinations at our hospital for several years.

By contrast with QUART (Veronesi), LAITT means:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>with Hivamat</th>
<th>without Hivamat</th>
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<td>IT = interstitial therapy (irradiation with 192Ir with the afterloading technique, performed intraoperatively by the operator during the same anesthesia)</td>
<td>43</td>
<td>32</td>
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<tr>
<td>T = percutaneous telecobalt therapy, c. 2-3 weeks following the operation</td>
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<td>16</td>
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<tr>
<td>LAITT QUART/segment</td>
<td>56</td>
<td>48</td>
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Table 1

Operating technique and Hivamat treatment

Results

The results following conservative therapy are compared for patients treated with Hivamat (n = 56) and for a control group (n = 48), as shown in Figures 1-6 (as of October 1990).

The statistical significance can be calculated for all six criteria under study.

Discussion

Conservative breast carcinoma therapy is gaining increasingly in importance today (12, 16, 20, 22, 29, 33, 38-40, 42). Such techniques assume close cooperation between experienced operators, pathologists, radio- oncologists and x-ray diagnosticians. They also require assuring the patient of reliable postoperative care, which - owing to the special problems entailed (radionecrotic fibroses) - cannot be delegated to inexperienced personnel.
Fig. 1:
Consistency

Fig. 2:
Pain and disturbances in sensitivity of the breast treated

Fig. 3:
Skin alterations (hyper- and depigmentation, pasty edema, erythrodermia, telangiectases, desquamation, epithelial lysis, necrosis)

Fig. 4:
Arm mobility, fine motor response
Engel and coworkers demonstrated an unequivocally positive correlation between the fear of recurrence and side effects of conservative treatment. Those patients without complaints had less feelings of anxiety (9).

The incidence of side effects correlates closely with the radicality of the operation (26, 46). Thus, for example, the formation of a lymphedema of the arm is related to the number of lymph nodes removed. The more conservative the surgical intervention, the better is the result from the cosmetic standpoint. In regard to women with small breasts, it is clear that one can hardly speak of conservative surgical intervention following a quadrantectomy or a large-scale segmental resection. Following a lumpectomy, the cosmetic-esthetic result is better, since just the tumor is cut away and thus only a narrow border of parenchyma must be sacrificed.

With more than 90% of our patients, treated according to the LAITT method, we were able to obtain a good or very good cosmetic result. This is in good agreement with the results reported by other groups (14,27,28).

A postoperative irradiation serves to eliminate residual tumorous matter in the remainder of the breast and possibly in the tumor bed. At the same time, this should be done with a view to minimum morbidity. Up to now, it remains unclear how large a selective dose is necessary, whether it is possible to dispense entirely with a booster dose and, if not, how large a minimum dose is required.

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The Harderand Laffergroup in Basel demonstrated the relationship between the number of lymph nodes removed and the formation of a lymphedema of the arm for postoperative irradiation of the lymph drainage paths [19]. That dispensing with the postoperative irradiation of the axilla and supraclavicular region can lessen the risk of a secondary lymphedema has also been shown by Kissin (26) and Engel and coworkers (19).

The side effects following conservative therapy are, furthermore, dependent on the extent of postoperative irradiation (14). At the 2nd "Early Stage Breast Cancer" Symposium in June 1988 in New York, Vilcoq (Paris) reported on the results found with 518 patients. The limit for a good cosmetic result was a skin dose of 68 Gy. Poor results were observed with an average superficial dose of 76 Gy (44). In 1988, Habibollahi and coworkers (Guy's Hospital, London) showed that skin doses above 50 Gy are observed at a later point in time (9, 14, 17, 45). Similar results were presented in a talk by Harris and coworkers (Boston) in 1988 in New York, with the recommendation to reduce the irradiation dose to 45 Gy for the entire breast and not to exceed a booster dose of 16 Gy for the tumor bed. Largely on the basis of the experience of the Hunig and Wahnergroup in Basel (24), as well as that of other centers (12,4,5,7,21,32,35,41,42), and also as a result of the recommendations made at the Consensus Conference in June 1985 in New York, we have modified our irradiation procedure to no longer irradiate the axilla and to irradiate the supraclavicular region only with pN 1 b and pN 2 patients. Centrally and medially located tumors require the additional irradiation of the parasternal lymph nodes.

On the other hand, the more restrained the surgical intervention, the more important a sufficiently intensive postoperative irradiation of the breast operated becomes. It is undeniable that adequate irradiation reduces the rate of recurrence in the breast operated. Fisher and coworkers (NSABP Study Report B-06), as well as Clark and coworkers, showed in good agreement that the local recurrence rate following conservative therapy without postoperative irradiation in an observation center over a period of up to 10 years amounted to nearly 30/% (6,11).

The local recurrence rates following conservative therapy and postoperative irradiation with observations of the course of treatment covering, in some cases more than 10 years are found to lie world-wide between 4 and 14% . For the patients treated in our clinic by the LAITT method, up to now the local recurrence rate over an average observation time of 32 months (maximum 61 months) amounts to 1.4%.

Lagos and coworkers (30,31) and also Fisher (10, 11) and Bahnson (3) were able to show that it is not possible to dispense with an irradiation even for DCIS, particularly for foci greater than 2.5 cm in diameter.

A direct comparison of the side effects found by the different groups is practically impossible, since different techniques were used on the breast itself and on the axilla and differences in irradiation management cannot be taken into account properly. Moreover, due to different procedures of calculation, the doses quoted cannot always be compared directly. It is also important to have more exact information about the point in time of the irradiation (the time elapsed since primary therapy or irradiation), since this represents an important parameter.

Finally, one may not forget that the evaluation of some side effects must take place more or less subjectively, unavoidable leading to some differences on the part of different authors and their different patient groups.

More or less strongly pronounced fibroses have been cited in the national and international literature with a frequency of 13-45% (9, 14, 17, 45). The most detailed study of these figures derives from Engel and coworkers. The results correlate well with our figures.

It appears to be important, to undertake countermeasures from the very beginning against a fibrosis and also against the formation of a lymphedema, since early alterations apparently can lead to serious complications over the next 10-15 years, whereas a low rate of side effects during the early stages does not give rise to later complications (34).

Evidently, a part of later fibroses and indurations in the breast is attributable to the postoperative formation of hematomas and seromas. Frischhiershows that, prior to radiation therapy, a mammography frequently indicates irregularly outlined compaction foci, which can be mistaken over many years for a carcinoma (15). Because of these operation- or irradiation-induced fibroses with scar tissue formation, only physicians having sufficient experience in the interpretation of such findings should perform the postoperative examinations. Indurations in the primary tumor region are frequently interpreted by inexperienced personnel as recurring tumors.

The results available until now from the treatment of patients with Hivamat indicate a marked reduction in side effects and therefore an optimal therapy by comparison with a control group comprising patients nottreated with Hivamat. The difference becomes all the more apparent in view of the fact that more patients in the Hivamatgroup were irradiated interstitially and percutaneously than in the control group (77%/0, compared with 67% in the control group), thus with a correspondingly higher dose than in the QUART group, so that a higher incidence of side effects was to be expected.

The rate and degree of severity of radiogenic fibroses and indurations could be lowered significantly for those patients treated with Hivamat (p<0.001).

Indurations were not observed, while the control group showed an incidence of 14% ! Similar results were achieved with respect to the other information documented.

Poorer cosmetic results, above all in regard to side effects of the skin, are observed with patients having very large and flabby breasts. Other authors have confirmed this observation (18, 44).

In regard to side effects occurring on the skin (hyperdepigmentation, telangiectases, edema, erythrodermia, desquamation, epithelial Iysis, necrosis), various authors have observed these with a frequency of between 10 and 27%, whereby it is necessary to point out that, by contrast with our evaluation, these results were as a rule observed at a later point in time (9, 14, 17, 45).

In the study of Engel, a total of 38% complained of pain in the breast treated (9). Our figures confirm this result. 6% of those patients not treated with Hivamat complained of pronounced or constant pain and 31% of moderate or occasional pain. The Hivamattreatment reduced these figures drastically (p<0.025, see Fig. 2).

Most frequently observed among our patients and also among those of Engel and coworkers (9) were various complaints and functional restrictions of the arm on the side operated. A pronounced restriction of the arm's mobility, as observed with 8% of our patients not treated with Hivamat and 4% of the patients in Engel's study, could no longer be objectified following Hivamattreatment, even on the 10th day postoperative.

With Hivamat, rapid fatigability, lessening of strength and pain in the arm could be further significantly reduced (p<0.025, see Fig. 5).

In regard to the occurrence of a lymphedema of the arm, a considerable scattering of observed frequencies has been reported in the literature, ranging from 3 to 30% (8, 9, 14, 17, 25, 27, 45, 45). The very different figures cited are due to the non-uniformity of treatment procedures, different evaluation criteria and definitions, and different operating techniques (number of lymph nodes removed).

54% of all benign lymphedemas of the arm form within the first year following axillary dissection and irradiation, two thirds of these during the first half year following therapy. Radiation damage in the form of radiofibroses is the most important complicating factor in the formation of lymphedemas (23).
An adjuvant chemotherapy, according to Engel and coworkers, also leads to negative effects (9). For these reasons, one should attempt to avoid combined damage by either operating on the axilla or administering radiation therapy (26, 37). Due to the pathophysiology, the method of choice for the therapy of a lymphedema of the arm, manual lymph drainage, can be combined with compression treatment and elevation (23). Diagnosis at the earliest possible moment in time or a prophylactic insertion greatly improves the prognosis for recovery and lessens the extent of later complications, such as a fixed lymphedema or elephantiasis (13). The use of such an edema prophylaxis can also reduce the cost of treatment considerably.

At our clinic, with Hivamat we were able to lower the rate of lymphedemas from 23% (4% severe, difference in size > 3 cm/19% moderate, difference in size 1-3 cm) to 7%. Severe lymphedemas have not yet been observed after treatment with Hivamat.

Contra-indications for a Hivamat therapy are acute arm vein thrombosis and acute erysipelas.

Fig. 8:
41 year-old patient; condition following LAITT, 10 days after concluding percutaneous postoperative irradiation (cobalt); treated with Hivamat

Fig. 9:
37 year-old patient; six weeks postoperative (LAITT) and two weeks after concluding percutaneous postoperative irradiation (cobalt); treated with Hivamat

Fig. 10:
69 year-old patient; condition following LAITT, three months postoperative and nine weeks after concluding percutaneous postoperative irradiation (cobalt); treated with Hivamat

Fig. 11:
The same patient as in Fig. 10

Fig. 12:
53 year-old patient; condition following LAITT, six months postoperative and four months after concluding percutaneous postoperative irradiation; treated with Hivamat
Conservative breast carcinoma therapy is, in view of its high psychological and cosmetic advantages, to be preferred, provided that this ensures the hygienization of the tumor site. It is furthermore to be hoped that the patient does not avoid preventive examinations due to the fear of having to submit to a breast removal or even remain silent in the face of a finding resulting from self-palpation.

The significance of side effects, which together with cosmetic aspects are of decisive importance for the quality of life of the patient should be given greater consideration today during the planning and operating phases, as well as the postoperative treatment, of conservative breast carcinoma therapy. A satisfactory cosmetic result and greatly reduced side effects are after all the very reasons for employing conservative procedures.

Typical side effects of radiation therapy following conservative breast surgery (QUART or LAITT), including axillary extirpation, are fibroses, pain or disturbances in the sensitivity of the breast operated, skin alterations (hyperpigmentation, depigmentation, edema, erythrodema), telangiectases, desquamation, epidermal lysis, necrosis, restrictions to movement of the arm including disturbances of fine motor response, pain, paresthesias, lessening of strength in the arm on the side operated, and a lymphedema. Hivamat is used for the rapid dissimilation of local edemas, for the dissolution of indurations of the connective tissue, for improving motional readiness, and for improving the flow equilibrium and permanence of pain relief.

The treatment represents a special form of manual lymph drainage, with which an oscillating electostatic force field builds up between the hands of the therapist and the body of the patient, giving rise to a vibrational and pumping effect which is still effective deep within the tissue. 15-20 minutes therapy daily are sufficient. Another particular feature of the Hivamat technique is that the lymph drainage can already be employed on the very first day postoperative, in order to restore lymph drainage after this has been damaged operatively or radiologically. It is our assumption that the rate of lymphedema occurrence following a prophylactic Hivamat lymph drainage will still be lower, even after 2-3 years.

Up to now, Hivamat-supported lymph drainage has shown significant improvements in the results for the following clinical criteria, compared with conventional manual lymph drainage: consistency; pain and disturbances to the sensitivity of the breast operated; skin alterations; arm movement; paresthesias in the arm and/or axilla of the side operated, and lymphedema.

### Literature


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