Crucial aspects of smoking in wound healing after breast reduction surgery

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Introduction

Cigarette smoking affects multiple organ systems. Besides an increased risk of various neoplastic, cardiac-, cerebral-, peripheral vascular and pulmonary diseases, smokers are more likely to have poor surgical outcome in general\(^5\). For a long time plastic and reconstructive surgeons have been blaming tobacco smoking for jeopardy of physiological wound healing and surgical outcome. In 1974, Sarin first demonstrated a 43% reduction in the blood flow of digits of normal volunteers, after smoking of a single cigarette\(^5,6\). Since 1977, when Mosely and Finseth first reported impaired wound healing of a wound of a smoker’s hand as well as a slow down of wound healing in ears of nicotine injected rabbits\(^7\), the literature has seen many cases and studies of delayed and impaired wound healing\(^8\)-\(^10\).

However, recommendations for smokers before surgery vary greatly. Some surgeons refuse to perform aesthetic or elective reconstructive surgery on individuals who use tobacco products\(^10\). Cigarette smoke contains more than 4000 toxic compounds\(^11\), of which nicotine is the toxin of greatest interest. Carbon monoxide and hydrogen cyanide are the two most common toxic gases.

Nicotine has several effects on wound healing. First, it causes a reduced proliferation of red blood cells, fibroblasts, and macrophages thus resulting in decreased tissue oxygenation and subsequent scar formation. Second, nicotine has been associated with increased platelet adheriveness causing microclots and decreased microperfusion\(^12\)-\(^13\). Nicotine also reduces levels of prostacyclin, one of the most important physiological vasodilatators\(^14\). Through these mechanisms, nicotine leads to tissue ischemia. Due to its 200 times higher binding-affinity to haemoglobin carbon monoxide induces formation of methemoglobin and decreases levels of oxygen available for tissue perfusion. Hydrogen cyanide inhibits the enzyme systems of major pathways of the oxidative metabolism and oxygen transport at the cellular level\(^15\).

All these processes in summary are responsible for poor surgical outcome in smokers. However, most of the hypoxic effects of smoking last no longer than 24 h after the last cigarette\(^13\)-\(^16\). Exception is the affinity of carbon monoxide to haemoglobin, which may last up to 48 h\(^17\). A single cigarette can initiate skin vasoconstriction for about 90 min\(^18\).

We evaluated the effect of smoking cessation after surgery on wound healing.
Patients and methods

Patients

In our prospective study we compared 25 nonsmoking patients and 25 smoking patients who were undergoing breast reduction in our unit between 2000 and 2003. We excluded patients suffering from systemic, immunologic, metabolic or hematologic disease to avoid the confounding effect on wound healing. All patients were informed preoperatively about the proposed negative impact of smoking and smoking cessation was recommended.

In 50 female patients, 25 smokers (mean age 39.4 years) and 25 nonsmokers (mean age 41.7 years), 93 breasts were reduced at our institution by two experienced plastic surgeons. In the group of the smokers 3 unilateral and 22 bilateral reductions were performed, in the group of the non-smoking women 4 patients received a unilateral and 21 patients a bilateral breast reduction. By chance the patients of the two groups were comparable by age and resection weight (table 1).

<table>
<thead>
<tr>
<th>Table 1. Demographics of the study group</th>
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<tr>
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<tr>
<td><strong>Number of patients</strong></td>
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<tr>
<td>Smokers</td>
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<tr>
<td>Age in years</td>
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<tr>
<td>- Mean (p=0.81)</td>
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<tr>
<td>- Range</td>
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<tr>
<td>Reduction weight in grams</td>
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<tr>
<td>- Mean (p=0.76)</td>
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<tr>
<td>- Range</td>
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The median reduction weight in nonsmokers was 534 g for each breast (lower quartile 180/upper 700). Smokers showed a median reduction weight of 512 g per side (195/ 900). There was no significant difference between the two groups concerning reduction weight (p = 0.76: Mann Whitney U Test). All patients received thrombosis prophylaxis starting 24 h before surgery until the 10th postoperative day (Lovenox 40 mg s.c. once per day).
Methods

Surgical procedure
Reduction mammoplasties were performed as central pedicle flap (Eren) or medial pedicle flap (Hall Findlay) techniques. The closure technique concerning breast-reduction is standardized in our institution. All surgeons used 4-0 Vicryl sutures for subcutaneous wound closure and 4-0 monocryl sutures for skin closure and did close both sides personally. Steristrips were used for additional dressing. We used one drain for each breast and removed them two days postoperative. No prophylactic antibiotics were used intraoperatively.

Wound healing
Regular wound healing was defined as presence of a stable and dry wound without inflammation or skin necrosis thus no longer requiring any dressing. Impaired wound healing was assessed as absence of the above criteria and the requirement of a wound dressing after the 10th postoperative day. The two operating surgeons assessed the surgical outcome and decided if further dressing was required after the 10th postoperative day. They did not know which patients were planned to be included in the presented study.

Cotinine measurements
To get objective data of the nicotine levels in smokers and nonsmokers, we measured urinary cotinine levels. Cotinine is a metabolite of nicotine, which is found in blood, urine and saliva. Cotinine has a half-life of nineteen hours. We determined urinary cotinine with a Cotinine-Urine ELISA-Test (DRG Cotinine MTPL EIA). The Urine samples were drawn preoperatively and on the fourth day after surgery.

Statistical analysis
Since data were not normally distributed (D’Agostino Pearson test), statistical analysis were performed using Mann Whitney U-test and Sign-test for independent or dependent data, as appropriate. For graphic comparison of the non-normally distributed data, we used box and whiskers plot presentation comprising median, 25th and 75th percentiles as well as outliers.

Results
Surgical procedure
In 12 nonsmoking patients and 14 smoking patients the Eren technique was performed, the Hall Findlay technique was used in 13 nonsmoking and 11 smoking patients.
Wound healing
Ten smoking patients showed impaired wound healing compared to only four patients of the non-smokers. Frequencies between groups were compared by one tailed Fisher test $p = 0.057$ (Fig. 1). We monitored the following wound healing problems: minor hematoma, minor wound dehiscence and partial infections.

In the nonsmokers group two patients operated by the Hall-Findlay technique showed wound-healing complications, compared to two patient operated by the Eren-technique. The group of smokers showed equal number of wound-healing complications - five in each group - in both groups of surgical techniques. Because of overall minor wound infections, no additional use of antibiotics and no further inpatient treatment was necessary. There was no need to perform any revision because of hematoma.

![Figure 1](image.png)

**Figure 1.** Incidence of impaired wound-healing in nonsmokers [NS] and smokers [S]

Cotinine measurements
The median preoperative cotinine level of smokers (S right 310 bar) was 1964 (783/3963) ng/ml, whereas preoperative cotinine level of nonsmokers (NS left bar) was 18 ng/ml (7/37) $p < 0.0001$.

Cotinine levels significantly decreased in both groups after a five day period. Smokers (S right bar) presented a median level of 432 ng/ml (148/1695) and nonsmokers (NS right bar) 15 ng/ml (4/34) $p < 0.0001$ Mann-Whitney-U-test (Fig. 2).

Smokers with regular wound healing (left bar ‘0’) presented a median preoperative cotinine level of 1614 ng/ml (294/4000), whereas smokers with impaired wound healing (left bar ‘1’) had a median preoperative cotinine level of 2117 ng/ml (883/3951) $p = 0.68$. Postoperatively smokers with regular wound healing (right bar ‘0’) showed a decrease to 389 ng/ml (23/2141), and smokers with impaired wound healing (right bar ‘1’) showed decreased levels of 485 ng/ml (345/935) $p = 0.60$. 
Cotinine levels between smokers with and without impaired wound healing showed a statistically significant difference between preoperative and postoperative values ($p < 0.05$) (Fig. 3). There was no significant difference seen between the two groups comparing the parameters age as well as reduction weight (table 2).

**Figure 2.** Urinary cotinine levels in [ng/cc] pre (left) – and post (right boxes)-operatively in smokers and nonsmokers.

**Figure 3** Urinary cotinine levels of smokers without (S0) and with (S1) impaired wound-healing, left bars showing preoperative cotinine levels and right bars postoperative levels.
Table 2. Differences between smokers with impaired and with regular wound healing

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<thead>
<tr>
<th></th>
<th>Smokers with regular wound healing</th>
<th>Smokers with impaired wound healing</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>15</td>
<td>10</td>
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<tr>
<td>Age in years</td>
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<tr>
<td>- Mean (p=0.79)</td>
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<tr>
<td>- Range</td>
<td>19.9-63.8</td>
<td>23.2-61.8</td>
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<tr>
<td>Reduction weight in grams</td>
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<td></td>
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<tr>
<td>- Mean (p=0.71)</td>
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<td>592</td>
</tr>
<tr>
<td>- Range</td>
<td>91-1555</td>
<td>62-1756</td>
</tr>
</tbody>
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Discussion

Many clinicians have presented their negative experience with smoking patients\textsuperscript{4,19-23}. A few experimental studies describe the negative impact of smoking on wound\textsuperscript{24} and bone healing\textsuperscript{25,26}. These effects are attributed to nicotine and the numerous other contents of cigarette smoke. Van Adrichem et al. proved that smoking of cigarettes jeopardises survival of free vascularised flaps in rats due to vasospasms in the flap pedicle that may not necessarily lead to complete flap necrosis\textsuperscript{27}. There is no consensus among plastic surgeons as to how long a patient should refrain from smoking before surgery.

Gill et al.\textsuperscript{28} showed an overall significantly higher incidence of breast complications with smoking (p = 0.0043). Smoking also caused a higher incidence of donor-site complications (p = 0.0033) and a higher incidence of fat necrosis (p = 0.0226), but no statistically significant correlation with partial flap loss and venous occlusion. O’Grady et al.\textsuperscript{29} described a trend for wound dehiscence, delayed healing and fat necrosis in large inferior pedicle reduction mammaplasties, although there was no statistically significant difference. Smokers were four times as likely to develop fat necrosis than nonsmokers. Finally there was no increase of complication rates among smokers with large reductions as opposed to smaller reductions. Padubidri et al.\textsuperscript{30} reports an overall complication rate in smokers of 439 39%, compared with 25% in ex-smokers and 26 in non-smokers (p = 0.002), who underwent breast reconstruction. Complications were significantly more frequent in smokers. From his point of view breast reconstruction should be done with caution in smokers. Smokers undergoing reconstruction should be strongly urged to stop smoking at least three weeks before surgery.
Glassman et al.\textsuperscript{31} presented comparable results: patients who quit smoking after spinal fusion surgery for longer than six months had a lower non-union rate (17\%) than smokers (27\%), but still a higher rate than nonsmokers (14\%). It was postoperative rather than preoperative smoking cessation that resulted in improved outcome. Akoz et al.\textsuperscript{19} reported a case of abdominoplasty with wound healing by secondary intention, because the patient was smoking immediately in the first postoperative days and a second case of a patient, undergoing breast reconstruction with a pedicled TRAM flap, who stopped smoking two years before surgery and started to smoke again the second postoperative day. Manassa et al.\textsuperscript{32} studied the effects of smoking in 132 patients who had undergone abdominoplasty. Smokers reported consuming, on average, 18 cigarettes per day. The rate of wound problems showed a statistical difference between smokers and nonsmoker (p < 0.01). 48 \% of the smokers showed wound healing problems before hospital discharge versus 18\% of the nonsmokers. Smokers should be informed about their possible higher risk of wound healing problems.

Former studies have shown that either active smoking (smoking a cigarette) or passive smoking (exposure to environmental tobacco smoke, ETS) has undoubtedly harmful effects on the cardio-vascular system\textsuperscript{33}. By measuring urinary cotinine it is also possible to correlate the nicotine levels in indoor air and the urinary cotinine to creatinine ratio of the passive smokers\textsuperscript{34}. Urinary cotinine levels are significantly higher in individuals exposed to ETS than non-exposed humans\textsuperscript{35} as seen in our study. Cotinine concentrations between smokers and nonsmokers differ by factor 10 to 100\textsuperscript{36}. The reduction of urinary cotinine levels in nonsmokers can be explained through the non-smoking environment in hospital. Usually nonsmokers are exposed to ETS, as outline above.

The present study can be seen as a pilot project to evaluate the impressive importance of smoking cessation in general and shows a tendency that even in smokers postoperative cessation of smoking appears to reduce complications in wound healing. To assess the benefit of only postoperative smoking cessation, further patients need to be included.

Smokers may maintain their normal smoking habits until hospitalisation and some refrain from smoking in the first postoperative days. The group of female smokers who did not develop any wound healing problems presented with lower cotinine levels before surgery and stayed more abstinent after surgery compared to the group of smokers who developed wound healing problems.

According to the results of our pilot project we conclude that each smoking patient scheduled for breast reduction surgery should be explicitly informed on the
beneficial effects of smoking cessation. If the patient is unable to quit smoking preoperatively she should be aware that even postoperative tobacco abstinence has a positive impact on the wound healing process.
References

19. Akoz T, Akan M, Yildirim S. If you continue to smoke, we may have a problem: smoking’s effects on plastic surgery. Aesthetic Plast Surg 2002;26:477.


