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CONTENTS

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Dear and beloved readers,

you just opened the last issue (or a double issue) of the year 2017. At the end of each year, it is a custom to look back over the past year or to look to the future and think about what is ahead of us in the future. I would also like to look in this editorial to the deep past as well as to the near future.

As a beginner in plastic surgery, I once had an idea that all unanswered questions, or at least their majority, could be properly answered on the basis of evidence-based medicine. It means that if we are not sure whether our patients are being treated properly, we can just search the literature, evaluate the articles found and decide on the appropriate treatment option, or perhaps do such study ourselves and prove that the chosen procedure leads or does not lead to the best results. I think it was a partly wrong idea.

It is true that we were able to accumulate and publish a huge amount of knowledge, but not always on solid scientific basis based on evidence-based medicine rules. One explanation for this may be that a large number of published papers still lack sufficient quality or they are not methodologically perfect. Perhaps we feel it subconsciously and therefore our decisions are still largely based not on evidence-based medicine but on our own preferences and experiences, or on the empirical experiences and recommendations of our teachers. Why is that and is it so bad?

Plastic surgery, maxillofacial surgery, aesthetic surgery as well as other surgical disciplines as such differ fundamentally from non-surgical disciplines such as internal medicine, oncology, neurology and other non-surgical disciplines. For non-surgical specialties, a number of robust, homogeneous, prospective, double-blinded and randomized studies, review articles, or meta-analyses are published that meet all evidence-based scientific criteria. They can afford the "luxury" to make decisions based on valid data and their treatment strategies can then be effective enough. However, are there similar "strong" studies also available for plastic surgery? And is it even possible to do such studies?

Factors that make it difficult to evaluate the effectiveness of different surgical procedures can be, for example, lacking homogeneity of the evaluated groups of patients. Patients enrolled in the treated and control group are not exceptionally different only in one, just evaluated and examined aspect or parameter. Too much heterogeneity in the group can then influence the conclusions of the study. Another problem in some less common diagnoses maybe the inability to collect a sufficient number of patients to provide general recommendations. It is even more difficult at all times to ensure that all patients in such a surgical trial are operated by equally experienced and qualified surgeons.

Not only these factors show us that perfection in plastic surgery cannot be achieved solely on the basis of evidence-based medicine. Of course, we need this kind of information, but we also need the expertise, insight and intuition of our much more experienced colleagues. Even knowing that opinions based on personal experience – "eminence-based" instead of "evidence-based" medicine may be incorrect or misleading, for example, when senior colleagues do not update their knowledge on an on-going basis and do not confront it with current knowledge. Even so, the daily interaction of surgeons with their experienced colleagues is an invaluable source of information for good clinical practice. I think it's just as important as the use of evidence-based knowledge.

Despite the above-mentioned doubts, we must use evidence-based medicine as a useful and important tool in our decision-making. However, we must not forget the knowledge, which is based on personal experience of our older colleagues. I wish you all, our readers, to be able to correctly balance both approaches. That is why we will continue trying to present not only the findings based on large randomized studies and evidence-based medicine but also the knowledge based on personal experience and our authors' own opinion. We are aware of the strengths and weaknesses of both approaches, but we trust your ability to deal with it.

Inspirational reading wishes

Aleš Fibír, M.D., PhD.
Editor-in-chief
Acta chirurgiae plasticae

PATIENT SATISFACTION AFTER BREAST RECONSTRUCTION: IMPLANTS VS. AUTOLOGOUS TISSUES

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ABSTRACT

Introduction: Breast reconstruction is increasingly present in the treatment of breast cancer. It may be accomplished with implants or autologous tissues. This cross-sectional study evaluates patients' satisfaction and quality of life in women after successful autologous or implant breast reconstruction.
Material and methods: 109 women who successfully underwent breast reconstruction between 2007 and 2016 were included. The patients completed the BREAST-Q questionnaire at follow-up visits. Additional data were collected retrospectively from the hospital charts regarding complications, smoking, chemotherapy, radiotherapy, unilateral or bilateral reconstruction, BMI and comorbidities. Mann-Whitney U Test was applied to evaluate differences between the autologous breast reconstruction group (n = 50) and the implant breast reconstruction group (n = 59).
Results: Women with a successful autologous reconstruction were significantly more satisfied with their reconstructed breasts than women with successful alloplastic breast reconstruction as measured by the BREAST-Q breasts module (p = 0. 00596), psycho-social well-being module (p=0.04) and sexual well-being module (p=0.00068). Furthermore, there is a higher degree of satisfaction in patients who have not undergone radiotherapy, with no complications and with a normal BMI for implant reconstruction group as well as in non-smokers, and bilateral reconstructions for flap reconstruction group.
Discussion: The findings of our study are in agreement with the data found in the literature, attributing greater satisfaction with physical, mental and social wellbeing, as well as with elements having repercussion on sexual wellbeing, to autologous breast reconstruction.
Conclusions: Autologous breast reconstruction leads to higher patient satisfaction than implant breast reconstruction. This study may help patients and medical teams in their decision-making process regarding breast reconstruction. This pilot study opens several questions that need further investigations in a larger prospective study

KEYWORDS

Breast reconstruction, breast-Q, satisfaction, implant, autologous tissue

INTRODUCTION

At present breast reconstruction is increasingly considered an integral part of the treatment of breast cancer. [1,2]

Other than physical, it offers to the reconstructed patients also the psycho-social satisfaction. This is the reason why, today, reconstructive surgery should be proposed to all women who will be/are having oncologic breast surgery.[3]

Due to the increasing number of patients seeking breast reconstruction, it is necessary to evaluate the impact of the results of reconstruction on the patients' quality of life.[4]

Basically, there are two different types of breast reconstruction: alloplastic reconstruction by tissue expanders and/or implants, or autologous reconstruction by pedicle or free flaps.

To obtain the best possible result, the two types of reconstruction can be used also in combination.

Flaps used in breast reconstruction are, either local (e.g LICAP – lateral intercostal artery perforator flap, AICAP – anterior intercostal artery perforator flap), regional (e.g LD – latissimus dorsi flap, TDAP – thoracodorsal artery perforator flap), distant (pedicled TRAM – transverse rectus abdominis flap) or free (e.g. DIEAP – deep inferior epigastric perforator flap, SGAP/IGAP – superior or inferior gluteal artery perforator flap, TUG – transverse upper gracillis flap etc.). In most patients the treatment is concluded with nipple reconstruction and areola-nipple complex tattoo.

In their studies many authors searched for the best technique of breast reconstruction.

Tam et al. analysed 63 articles to compare results obtained in terms of breast reconstruction.[5] He found a consensus in the literature on higher patient satisfaction with autologous reconstruction. On the other hand, however, he found that breast reconstruction by implants was by far more

popular. This fact can be explained by greater complexity, invasiveness as well as longer hospital-stay and rehabilitation after autologous reconstruction.

Damen et al. found that 90% of women reconstructed by DIEAP flaps perceived the reconstructed breast as their own.[6]

Fischer et al. report that free flap reconstructions needed fewer surgical procedures, the complications and failures were not frequent and the patients required fewer clinical visits and reached a complete result faster than patients reconstructed with expanders/implants.[7]

Tsoi et al confirmed this evidence.[8] They found that the infection rate and operation failure rate (removal of the implant), was higher in patients reconstructed with implants compared to those reconstructed with autologous tissue. The risk factors associated with failure of reconstruction include smoking, obesity, paucity of donor tissues and type II diabetes mellitus (DMII).[9,10]

Ohkuma et al. showed improvement of the quality of life postoperatively after both autologous and alloplastic breast reconstruction.[11] However, they also found that autologous reconstruction was associated with a higher rate of functional impairment.

Macadam et al. studied the alloplastic breast reconstruction and showed that silicone implants were associated with greater satisfaction with breast reconstruction outcome (physical, psychological and sexual).[12]

This was confirmed by McCarthy who stressed also the negative effects of radiotherapy on reconstructed tissues.[13]

Reaby et al. and Ng et al. showed that some women refused breast reconstruction, which could be explained by advanced age, their greater fear of a second operation, but also with problems in communication with their surgeon.[14,15]

Regarding the last, Ho et al. showed that a woman satisfied with the communication with the surgeon was also happier with the final aesthetic result of reconstruction.[16]

The aim of our study is to investigate which technique of breast reconstruction (by alloplastic or autologous technique), offered the highest quality of life to the patients. For this reason, we surveyed all women who experienced a successful breast reconstruction at our institution between 2007 and 2016. We used the BREAST-Q patient-reported outcomes measurement as the primary instrument to measure their quality of life and satisfaction with the outcomes.

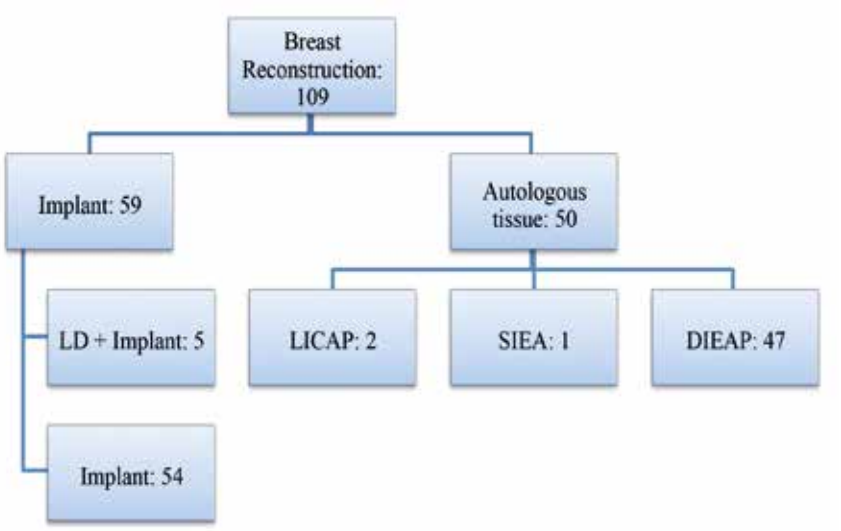

Fig. 1. The group of patients in the study

MATERIAL AND METHODS

This study was aimed at all patients who underwent breast reconstruction after mastectomy at the University Hospital "ASUITS" in Trieste, between 2007 and 2016.

The patients were divided into two groups: alloplastic reconstructions (with or without a flap) and autologous reconstructions.

The initial cohort of patients was composed of 98 patients reconstructed with a DIEAP flap, 137 reconstructed with implants, 16 with latissimus dorsi flap only and 19 with latissimus dorsi flap and an implant.

Only the patients who had successfully completed the reconstruction were included into the study.

From this reason we excluded all patients who had had complications in terms of failure of the reconstructive procedure such as loss of the flap or the implant.

The full completion of breast reconstruction means reconstruction of the breast mound with or without nipple-areola complex reconstruction or contralateral adjustment.

Excluded from the study were also women who did not sign the informed consent form, did not attend outpatient clinics until removal of all sutures and women with psychiatric disorders.

IMPLANT	Average age	Minimum	Maximum	AUTOLOGOUS TISSUE	Average age	Minimum	Maximum
0-6 Months	53	30	76	0-6 Months	54	46	67
6-12 Months	60	40	70	6-12 Months	60	39	77
1-3 Year	58	43	77	1-3 Years	59	46	74
3 and more	55	31	71	3 and more	56	37	74

Table 1. Patient's age distribution for each time intervals at the reconstruction

IMPLANT	Average age	Minimum	Maximum	AUTOLOGOUS TISSUE	Average age	Minimum	Maximum
0-6 Months	53	30	76	0-6 Months	54	46	67
6-12 Months	60	40	70	6-12 Months	60	39	77
1-3 Years	60	44	80	1-3 Years	61	48	76
3 and more	60	34	71	3 and more	62	45	76

Table 2. Patient's age distribution for each time intervals at the Breast-Q questionnaire

		Implant	Flap
Smoking	Ex smoker	8%	8%
	Non-smoker	78%	90%
	Smoker	14%	8%
CT	CT	37%	28%
	CT neo-adjuvant	3%	4%
	CT in treatment	0%	2%
	no CT	63%	66%
	CT Previous	0%	10%
RT	RT	7%	14%
	RT neo-adjuvant	2%	0%
	no RT	85%	74%
	RT previous	7%	10%
Hypertension		3%	4%
Dyslipidemia		5%	0%
Diabetes		0%	2%
NAC	Reconstructed	27%	26%
	No NAC	5%	2%
Reconstruction	R. Unilateral	3%	4%
	R. Bilateral	78%	92%
	Relapse	22%	6%
	Prophylactic	5%	0%
BMI	BMI 18,5-24,9	25%	36%
	BMI 25-29,9	3%	12%
	BMI < 30	0%	2%
Complications	Major	20%	24%
	No complications	63%	52%
	Minor	22%	34%

Table 3. Distribution of smoking, CT (chemotherapy), RT (radiotherapy), hypertension, dyslipidemia, diabetes, NAC (nipple areola complex), reconstruction, BMI (body mass index), complications for each groups

The study involved patients seen for follow-up visits at the Plastic and Reconstructive Surgery Unit of Cattinara Hospital, from November 2015 until April 2016.

109 patients were enrolled into the study, 59 (54%) women were reconstructed with implants and 50 (46%) with autologous tissues (Fig.1).

The BREAST-Q patient-reported outcomes measure was used to evaluate the outcome of breast reconstruction as perceived by the patients.[17]

BREAST-Q questionnaire is one of the few instruments in reconstructive breast surgery that satisfies the international standards in terms of development and validation.

The aim of BREAST-Q is to evaluate the impact of breast reconstruction on quality of life and satisfaction from the patient's perspective.

We used the BREAST-Q postoperative reconstruction module (https://eprovide.mapi-trust.org/), consisting of

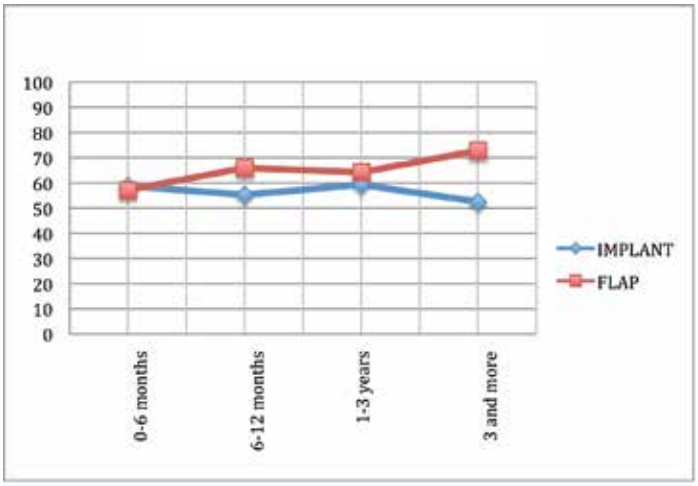

Fig. 2. Satisfaction with breast

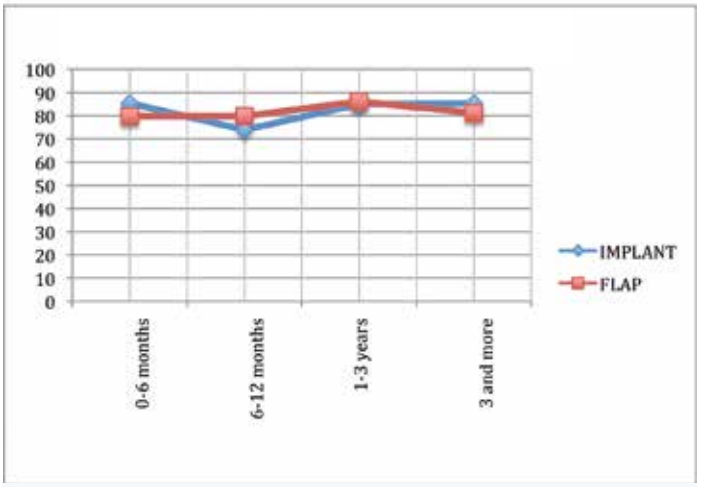

Fig. 3. Satisfaction with outcome

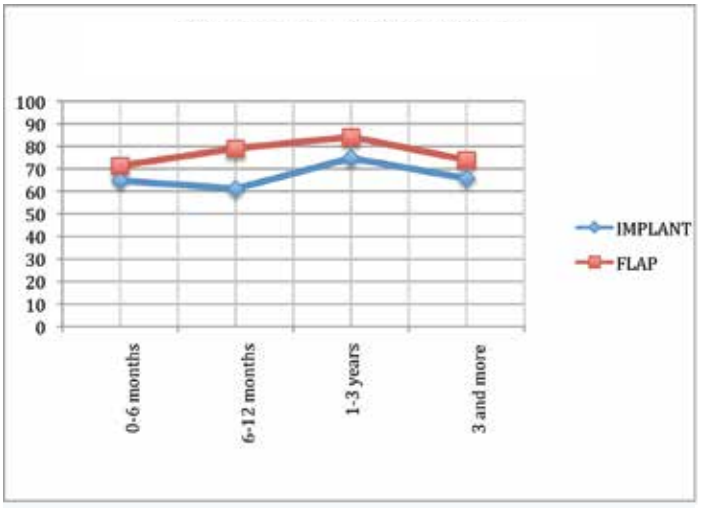

Fig. 4. Psychosocial wellbeing

nine scales. Each one consists of three to five items using a Likert scale.

The score obtained from each scale is transformed into a 100-point scale, where 0 means very dissatisfied and 100 very satisfied.

The score transformation is made by a free software available at the same Internet website.

By using BREAST-Q it is possible to evaluate the quality of life in terms of psychosocial, sexual and physical wellbeing as well as satisfaction with outcomes of breast reconstruction and information.

All scales have a good internal consistency (Cronbach alpha varies from 0.88 to 0.97).[3]

The two groups were divided according to the time passed from surgery, to assess if and how it affected the overall satisfaction of patients. We divided the patients into four time intervals: 0–6 months, 6–12 months, 1 to 3 years and more than 3 years after reconstruction.

For each patient we analysed her medical history (other surgical treatments, radiotherapy, chemotherapy, age at the reconstruction and at the questionnaire (Table 1, Table 2), body mass index (BMI), comorbidity, and smoking (Table 3). We also divided complications into major – those requiring operative interventions (e.g. postoperative thrombotic event, flap loss, haematoma) and minor – requiring non-surgical therapy (cellulitis, seroma, infections).

The second phase of the study focused on assessing possible interactions between the reconstructive techniques and previously described variables.

We studied the two groups in relation to the score obtained in the test: satisfied patients (score ³ 60/100) and those not satisfied (<60/100).

Descriptive statistics was used to describe baseline characteristics, for which the women were analysed according to their autologous or implant breast reconstruction.

For each time interval we calculated the mean BREAST-Q score and we used Mann-Whitney U test for statistical analysis. A value of $p < 0.05$ was used to indicate significance.

RESULTS

Satisfaction with the reconstructed breast

Fig. 2 shows that the mean satisfaction with breast reconstruction in the first time period was the same but as time passed the satisfaction of the patients treated with autologous tissue improved while the satisfaction with the reconstruction by implants decreased.

We noticed higher values of satisfaction in the time period beyond 3 years with autologous reconstructions, which is in accordance with the fact that the flap requires a longer time to settle completely than the implant. On the other hand, satisfaction with implant based reconstruction in that time period started to decrease, probably because of the onset of im-

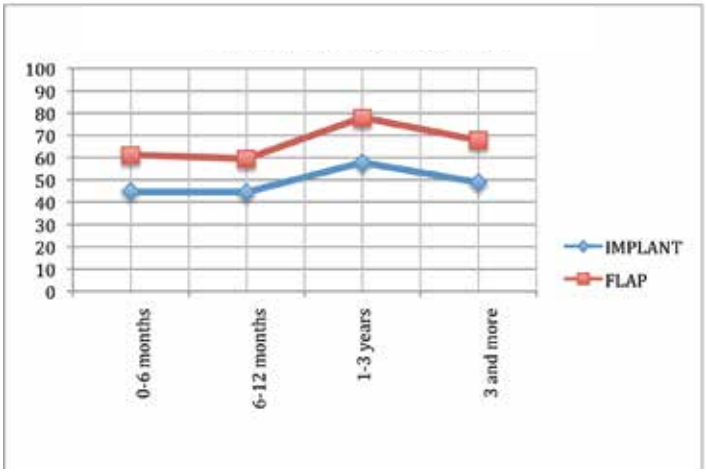

Fig. 5. Sexual wellbeing

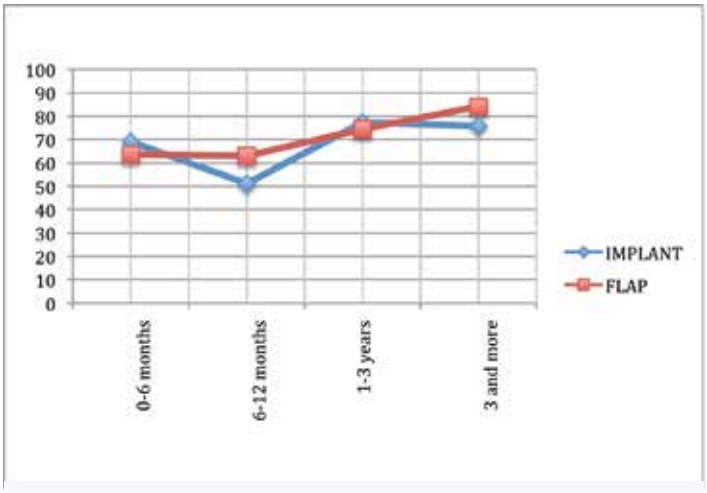

Fig. 6. Physical wellbeing: Chest

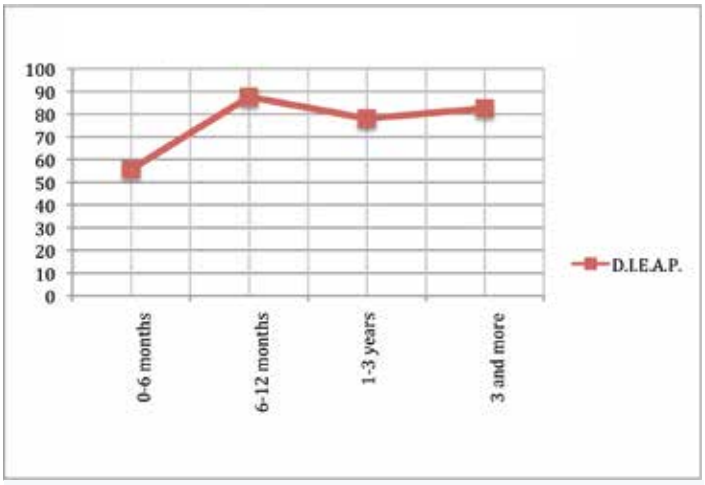

Fig. 7. Physical wellbeing: Abdomen

plant-related complications such as the capsular contracture.

Statistical analysis confirmed the initial assumptions (p=0.00596).[4,18-21]

Satisfaction with the outcome

Fig. 3 describes the satisfaction with the outcome. Our data showed no difference between the two mean satisfactions (p=0.58).

This evidence doesn't confirm the initial assumption of higher satisfaction in patients treated with autologous tissue reconstruction.[19]

Psycho-social wellbeing

The analysis of psychosocial wellbeing showed that the autologous tissue reconstruction offered higher satisfaction compared to that with implants (p=0.04).

Fig. 4 shows that the mean satisfaction of patients reconstructed with implants was lower compared to the autologous one, but in the last time period both of the curves pointed down. This might be due to the older age of patients in this phase, as described in Tables 1 and 2.

Sexual wellbeing

Fig. 5 describes the sexual well-being. It can be clearly seen that the autologous tissue offers a higher satisfaction than an implant (p=0.00068). We agree with the data in the literature indicating that flaps need a longer time to achieve the maximum degree of satisfaction but, at the end, this is higher than satisfaction with implants.[19]

It is interesting that in the last time period both techniques show the same trend as in Fig. 4.

We report that 9% of women from both groups decided to tick "not applicable" to confirm that the age can influence sexual wellbeing.

Physical wellbeing: Chest

The analysis noticed no statistical difference between the two techniques (p=0.4413).

Our results do not agree with the data from the literature that quote a higher satisfaction rate for reconstruction with autologous tissue.[23]

It is important to stress that both techniques show a positive trend. (Fig.6.)

Physical wellbeing: Abdomen

BREAST-Q can analyse the physical wellbeing regarding the abdomen for DIEAP and TRAM flaps. Our patients treated with DIEAP flaps experienced a high satisfaction with their abdomen after surgery with a positive trend with time.

Our data do not agree with literature that quotes a 52% of satisfaction; in our population it is higher. (Fig. 7.)[24]

Satisfaction with information, surgeon and staff

The last part of questionnaire analyses the satisfaction with information given to the pa-

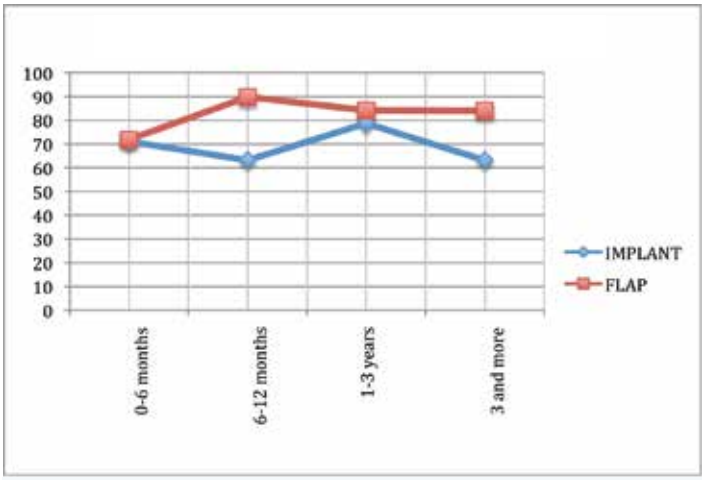

Fig. 8. Satisfaction with Information

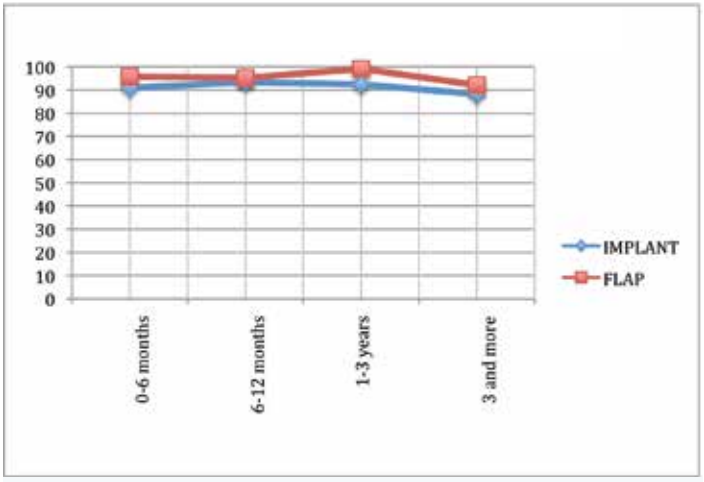

Fig. 9. Satisfaction with surgeon

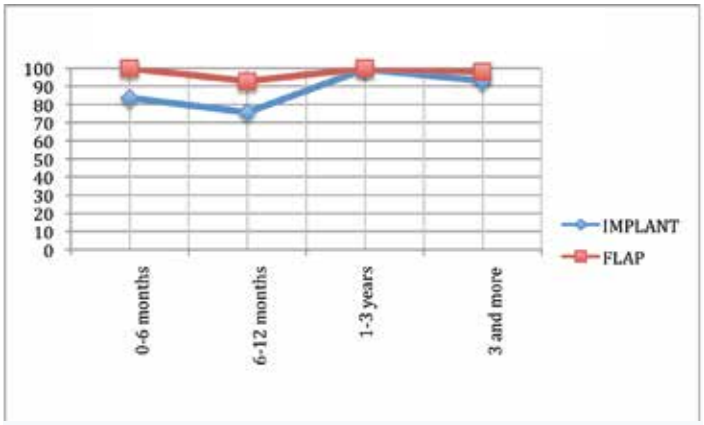

Fig. 10. Satisfaction with staff

tient by the surgeon and the staff. The data are shown in Fig. 8, 9 and 10.

The statistical analysis shows a significant difference between the two groups in satisfaction with information (p=0.0003). There is no significant difference in satisfaction with surgeon (p=1) and staff (p=0.23). In our institute we evidenced a satisfaction level close to 100% in this questionnaire module.

Our data agree with the data from the literature and show how a woman patient satisfied with her relationship with her surgeon will be more satisfied with her reconstructed breast.[15,19]

Results of the 2nd phase

We studied in detail the data about satisfaction with the reconstructed breast because the first phase of our study showed a statistical difference. Our analysis noticed that in the autologous group 52% of patients were satisfied compared to only 41% in the implant group.

Furthermore we found a higher degree of satisfaction in patients with implants that have not undergone radiotherapy, had a normal BMI and were without complications, as well as in patients with autologous reconstruction if they were non-smokers, or had a bilateral reconstruction.

It is interesting that the patients with unilateral reconstruction were more dissatisfied.

DISCUSSION

The findings of our study are in agreement with the data found in the literature, attributing greater satisfaction with physical, mental and social wellbeing, as well as with elements having repercussion on sexual wellbeing, to autologous breast reconstruction.[25-33]

We found a significant difference in the quality of life after autologous breast reconstruction and reconstruction by implants.

Our study shows no significant difference between the two techniques concerning satisfaction with outcome, physical wellbeing regarding chest and relationship with the surgeon.

Bresser et al. showed that almost half of the patients treated with implants felt their reconstructed breasts as not being "their-own".[31]

This is confirmed by our study that describes how the autologous tissue reconstruction shows a positive trend in satisfaction with breast with time, while breast reconstruction by implants shows a negative trend with time.

This might be due to the fact that the use of implants might need several re-operations or even implant replacement for the capsular contracture.

For this reason, Drazan et al., recommends reconstruction by autologous tissue, specifically the DIEAP flap, because it allows achieving a more stable and lasting satisfaction with time.[34]

Satisfaction with Breasts		Implant			Flap		
		Satisfied	Not Satisfied	p	Satisfied	Not Satisfied	p
Smoking	Ex smoker	13%	6%	0.09	3%	13%	//
	Non-smoker	75%	80%	0.0001	90%	79%	0.0001
	Smoker	13%	14%	0.01	7%	8%	0.007
CT	CT	33%	40%	0.0001	21%	33%	0.0004
	CT neo-adjuvant	4%	3%	0.01	0%	8%	//
	CT in treatment	0%	0%	//	3%	0%	//
	No CT	67%	60%	0.0001	76%	46%	0.0001
	CT previous	0%	0%	//	7%	13%	0.069
RT	RT	8%	6%	0.116	7%	21%	0.015
	RT neo-adjuvant	4%	0%	//	0%	0%	//
	No RT	88%	83%	0.0001	69%	71%	0.0001
	RT previous	0%	11%	//	10%	8%	//
Hypertension		4%	3%	//	3%	4%	//
Dyslipidemia		0%	9%	//	0%	0%	//
Diabetes		0%	0%	//	3%	0%	//
Reconstruction	Unilateral	75%	80%	0.0001	79%	96%	0.0001
	Bilateral	25%	20%	0.0024	7%	4%	//
	Relapse	0%	9%	//	0%	0%	//
	Prophylactic	4%	6%	//	3%	0%	//
NAC	NAC	21%	31%	0.001	28%	21%	0.0002
	No NAC	0%	6%	//	7%	0%	//
BMI	BMI 18.5-24.9	88%	60%	0.0001	50%	54%	0.0001
	BMI 25-29.9	13%	34%	0.004	35%	38%	0.0001
	BMI <30	0%	6%	//	15%	8%	//
Complications	Major complication	4%	31%	//	28%	17%	0.0072
	No Complication	83%	49%	0.0001	45%	54%	0.0001
	Minor complication	13%	29%	0.013	31%	33%	0.0025

Table 4. Distribution of smoking, CT (chemotherapy), RT (radiotherapy), hypertension, dyslipidemia, diabetes, NAC (nipple areola complex), reconstruction, BMI (body mass index), complications for each groups divided in satisfied and not satisfied

The feeling that the autologous tissue is able to achieve a stable, long-lasting reconstruction, obviously, influences the sexual, physical and psychosocial wellbeing positively.

We agree with the findings in the literature that patients reconstructed by autologous tissue have higher satisfaction rates compared to those with reconstruction by implants but on the other hand the satisfaction with the reconstructed breast is influenced also by the way in which the woman faces the cancer.[35]

It is true that reconstruction by flaps, especially, if microsurgical, is technically more demanding than the one by implants, but it is also true that this technique allows for a single stage reconstruction, with psychological and aesthetic benefits.[33,36]

These features probably affect the satisfaction, especially shortly after reconstruction.

In the module "satisfaction with outcome" BREAST-Q evaluates if the patient has repented of her choice and how the reconstruction had changed her life.

We want to stress that in both groups women didn't change their mind and they were still happy with the outcome.

Ho et al. showed the importance of communications and the relationship with patients for achieving high satisfaction rates.[16]

In our institute we noticed a satisfaction rate close to 100%.

The literature reports a lot of variables that could be associated with satisfaction, so we analysed them in the second phase of our study.[37]

The data suggests a significant difference between the satisfied patients and those who are not satisfied.

This evidence could be a starting point for other studies to analyse the relationship between the variables and the satisfaction (Table 4).

We found that there were more satisfied women in the implant group if they hadn't had complications, if they had a bilateral reconstruction, if they had no radiotherapy and if they had a normal BMI.

If we analysed patients reconstructed by autologous tissue and with a BMI > 30, we were able to notice that there were more satisfied patients than unsatisfied patients in this group.

Smoking can be a risk factor for satisfaction; in fact non-smokers are more satisfied than smokers.

Our data show that autologous tissue breast reconstruction needed more secondary corrections compared with reconstructions with implants (32% vs. 16%).[4]

We noticed more complications in patients treated with radiotherapy versus patients not treated, also in patients with autologous tissue reconstructions.

No significant difference was seen between the two groups for the middle age women.

As described in the literature, immediate breast reconstruction is preferred when possible.[36]

In our unit all patients treated by autologous reconstruction had immediate reconstruction, while only 8 women treated with implant had an immediate reconstruction, the other had a two-stage tissue expander-to-implant reconstruction.

We excluded women with implant or flap failure.

This might be considered a drawback, but we agree with data from the literature that their quality of life represents features of a different process compared with patients after a successful breast reconstruction.[4] We did not distinguish between unilateral and bilateral breast reconstruction within the breast reconstruction groups.

Most likely, our cohort of patients entering the study was too small for significant results to be detected, so we consider this study a pilot study in preparation for conducting a larger, prospective study.

CONCLUSIONS

Women after a successful breast reconstruction are generally satisfied and have a good quality of life. This study investigated which surgical technique was associated with better outcomes according to the patients. We confirm that autologous breast reconstruction allows achieving a higher degree of satisfaction than implant breast reconstruction. We found no difference in the quality of life between the autologous and implant techniques.

The conclusions of this study may be interesting for professionals dealing with breast reconstruction. This may helps patients and surgeons in making informed decisions for breast reconstruction. To strengthen the evidence regarding satisfaction with the entire breast procedure, it is necessary to perform prospective studies with larger and more homogeneous groups.

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OLEOGEL-S10 TO ACCELERATE HEALING OF DONOR SITES: MONOCENTRIC RESULTS OF PHASE III CLINICAL TRIAL

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ABSTRACT

Aim: The aim of this study was to demonstrate the efficacy of a new topically applied gel in accelerating re-epithelialization of donor sites.
Material and methods: Oleogel-S10, an ointment containing betulin-rich triterpene dry extract from birch bark was tested in an open, blindly evaluated, prospective, controlled, randomized multicentre study to improve wound healing in donor sites. The primary endpoint was time to wound closure, and secondary endpoints were scar related measurements at the time of wound closure, and 3 and 12 months after wound closure (POSAS, laser speckle contrast analysis, viscoelastic analysis).
Results: We report the results from a single centre (Department of Burns and Reconstructive Surgery, University Hospital Brno) of this phase III clinical trial. A total of 32 patients (25 men and 7 women) were included with the mean patient age of 41.8 years (SD, ±11.66). The mean extent of patient's donor sites in the study was 56.77cm2 (SD, ±20.39). Median healing time of the verum group (Oleogel-S10) was 7 days (95% Confidence Interval 7–8 days) and for controls 8 days (95% CI 7–10 days). Comparison of POSAS data from the verum group revealed significantly lower values at all three time points as compared to the controls. Perfusion of scars of the verum group reached on average of 115 perfusion units at the end of treatment; the average was 69.8 perfusion units at the 3-month follow-up and 50.2 perfusion units at the 12-month follow-up. Control sites displayed significantly higher values at all time points (122.2 perfusion units, 73.9 perfusion units, 52.2 perfusion units). Significant differences were detected in the skin's viscoelastic properties, with sites treated with Oleogel-S10 displaying more favourable values.
Conclusion: In our results, we demonstrate the significant effectiveness of Oleogel-S10 in donor sites healing

KEYWORDS

Donor site, Triterpenes, Oleogel-S10, wound closure

INTRODUCTION

During the recent years was observed substantial progress in the quality of care provided to burn patients. Such progress concerns antimicrobials and systemic therapy, but in particular wound management. For burn patients whose therapy includes split-thickness skin grafting, wound management concerns both burn and donor sites.[1] Particularly in patients with critical burns, donor sites are often lacking and therefore any possibility to accelerate epithelialization and to minimize scarification is beneficial for both patients and personnel providing treatment.[2]

The time period for donor site healing is one of the most important factors responsible for duration of hospitalization. For patients with critical burns, this means shortening the time of donor site epithelialization, shortening the interval between two harvests from a single site, and earlier closure of large areas, from which necrotic skin has been removed.

If no complications occur, the meantime period for donor site healing is around 2–3 weeks. Infectious complications in particular interfere with the transition of healing phases and prolong healing. Healing with complications is also subject to increased risk of developing hypertrophic scars.[3]

MATERIAL AND METHODS

Study design and treatment

The project was officially entitled Open, Blindly Evaluated, Prospective, Controlled, Randomized, Multicenter Phase III Clinical Trial to Compare Intra-individually the Efficacy and Tolerance of Oleogel-S10 versus Standard of Care in Accelerating the Wound Healing of Split-Thickness Skin Graft Donor Sites. This phase monitored a total of 105 patients from various European centres.[4] 32 patients (30.5%) from these were included in prospective monitoring

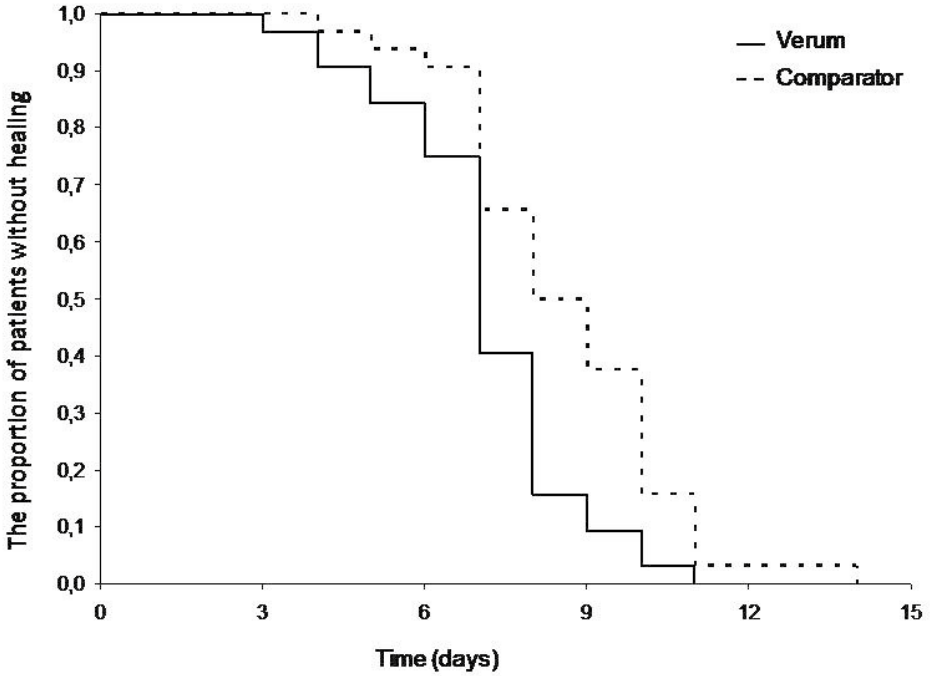

Fig. 1. Median healing time (95% confidence interval). Verum 7 days (7–8), comparator 8 days (7–10). *P*-value based on the Cox model with random effects: 0.003

at the Department of Burns and Reconstructive Surgery, University Hospital Brno. This article focuses on the results of the treatment phase and 1 year of follow-up. This experiment was carried out with the approval of the Ethics committee of the University Hospital Brno provided on 27 June 2012. All patients provided their informed consent prior to enrolment to the study. The entire project was carried out while respecting the Principles of Good Clinical Practice (GCP).

The primary endpoint was intra-individual difference in time to wound closure (at least 95% epithelialization) between wound halves either treated with Oleogel-S10 and non-adhesive wound dressing or treated with non-adhesive wound dressing alone, based on blinded photo evaluation by three independent blinded experts.

Study protocol

Following split-thickness skin graft (STSG) collection (Zimmer® Air Dermatome) was the donor site photographed and a computer and the internet were used to split the site randomly into two halves. An STSG was harvested from the thigh or buttocks of each patient at uniform thickness of 0.20 mm. The first half was designated as verum and was treated with both Oleogel-S10 and a Mepilex non-adhesive wound dressing (Mölnlycke Health Care, Norcross, GA, USA), and the other half was treated following standard of care (SOC) with Mepilex only without any ointment. At each change of dressing was taken photographic documentation and the wound's epithelialization extent was assessed. Swabs for microbiological monitoring were also collected. The wound was handled in this manner until it healed completely (at least 95% epithelialization). This was followed by monitoring at 3 and 12 months following STSG collection.

Assessment

Assessments of effectiveness (time to wound closure) and cosmetic effect were carried out for the two compared sites at the end of treatment (EOT), a 3-month follow-up (3m-FU), and a 12-month follow-up (12m-FU). To achieve optimal assessments, we used the Patient and Observer Scar Assessment Scale (POSAS). Laser speckle contrast analysis (LASCA) was carried out at all monitoring phases and the skin's biomechanical properties were analysed after 12 months. Viscoelastic parameters were analysed. The R0–R9, F0, F1, and Q0–Q3 parameters were monitored. Table 1 shows the most important R, F and Q parameters and their meanings. For more objective results, only one physicians measured cutometric and perfusion parameters. The same physician was the observer in POSAS.

POSAS is currently one of the most frequently used assessment scales.[5] Due to its universality and high objectivity it is used for many scars arising from various types of wounds. This scale is divided into two parts. The observer scale comprises six indicators (vascularity, pigmentation, thickness, relief, pliability, and surface area). Patients respond to seven questions concerning such parameters as pain, the irregularity of the scar, and colour differences. Each indicator and question is scored on a scale from1 to 10, with 1 representing the best result and 10 the worst.

LASCA (laser speckle contrast analysis) is a very sensitive method used to monitor differences in blood perfusion.[6] It is a non-invasive method where by a laser beam is used to detect blood perfusion in the microcirculation of the skin and subcutaneous tissue. It measures blood flow at an average depth of 0.5–1.0 mm. Data was measured using the PIMsoft (Perimed, Sweden) software analysis tool. This method is primarily useful for early assessment of burn site's depth,

although it can also assess very precisely the quality of perfusion surrounding and wound already healed, and thereby reveal sites at risk for hypertrophic scars. LASCA was carried out three times: at EOT, 3m-FU, and 12m-FU.

The Cutometer® MPA 580 (Courage+Khazaka electronic GmbH, Cologne, Germany) is an instrument used to measure skin's viscoelastic properties.[7,8] The device creates negative pressure, which is variably configurable between 2 and 50 kPa, and operates based on skin suction. During measurement, the selected skin site is drawn in to the probe's aperture. The depth the skin penetrates into the aperture is measured through a contactless optical system. The skin's biomechanical properties were measured at 12m-FU. A probe with a 2mm aperture was used, and constant negative pressure of 45 kPa was applied for all measurements. On-time was 2s and was followed by off-time (relaxation time) of 2s. The measurement was repeated three times. For each patient, two points on the verum half and two points on the control half were selected. The measurement was repeated four times at each point, i.e. 48 measurements were performed for each patient. Resulting values were then averaged for each point. The acquired parameters could then be interpreted as several indicators, such as skin extensibility (Ue), delayed distension (Uv), final deformation (Uf), immediate retraction (Ur), total recovery (Ua), and residual deformation at the end of measuring cycle (R).

Statistical analysis

Means with standard deviations were adopted as descriptive statistics for the evaluated parameters as well as for their differences in time, between treatments, and between observers. The statistical significance of differences was analysed using the Wilcoxon paired test. Time to healing was visualized using Kaplan–Meier analysis and described by median survival and its 95% confidence interval; the statistical significance of the difference between treatment curves was tested by means of the Cox proportional hazards model with random effects. Statistical analysis was conducted using SPSS 22.0.0.1 (IBM, Armonk, NY, USA).

RESULTS

A total of 32 patients were included from the Department of Burns and Reconstructive Surgery, University Hospital Brno. There were 25 men and 7 women and mean patient age in the set was 41.8 years (SD, ±11.66). A total of 31 patients had been hospitalized with burns, and only 1 patient was hospitalized for closure of a wound following free-flap surgery. The mean extent of patients' donor sites in the study was 56.77 cm^2 (SD, ±20.39). Two patients did not come for follow-ups, consequently 30 patients went through the entire protocol.

Donor site healing time

On average, donor sites treated with Oleogel-S10 healed completely in 10.03 days and control sites in 11.09 days. Median healing time for experimental sites was 7 days, and for comparator sites it was 8 days. Median healing time (95% confidence interval), verum 7 days (7–8), comparator 8 days (7–10). P-value based on the Cox model with random effects: 0.003. Fig. 1 displays the median healing time of donor sites for patients in the set. Fig. 2 presents real photographic documentation within donor site wound healing.

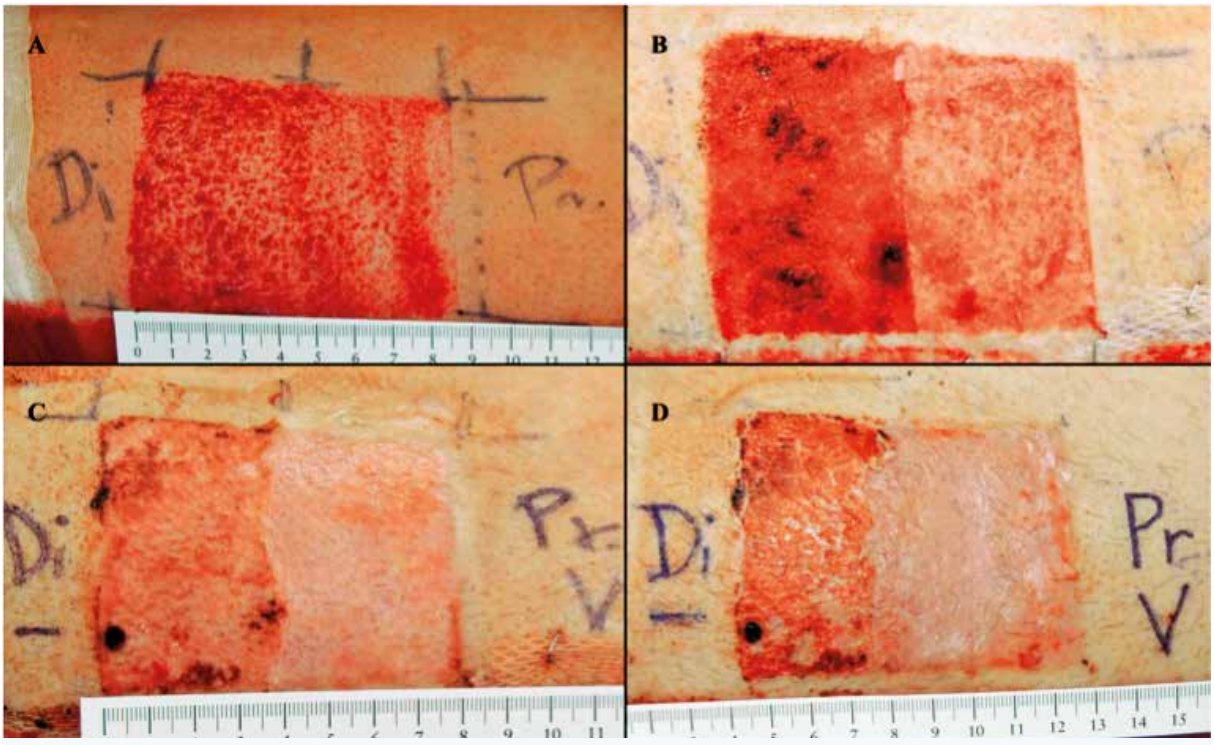

Fig. 2. Donor site wound healing (Pr.– proximal part with application of Oleogel-S10). A – Immediately after surgical procedure, B – 2nd day post procedure, C – 7th day post procedure, D – 9th day post procedure – complete wound closure (end of treatment)

- **R0** = Uf (first maximum amplitude – final deformation)
- **R1** = Uf –Ua (first minimum amplitude, ability to return to original state)
- **R2** = Ua/Uf (viscous deformation)
- **R3** = final maximum amplitude
- **R4** = final minimum amplitude
- **R5** = Ur/Ue (elasticity in the curve without viscous deformation)
- **R6** = Uv/Ue
- **R7** = Ur/Uf (so-called biological elasticity)
- **R8** = Ua (redeformation ability)
- **F1/F2** = area above the curve (the more elastic, the less area there is)
- **F3 =** area within the curve (skin fatigue)
- **F4 =** area beneath the curve (skin firmness)
- **Q0 =** maximum recovery area
- **Q1 =** total recovery
- **Q2** = elastic recovery
- **Q3** = viscoelastic recovery

Table 1. Examined R parameters for patients in the set

The scar assessment included repeated use of POSAS (at EOT, 3m-FU, 12m-FU). On the patient scale, the verum half recorded decreasing means of 12.1 points at EOT, 9.0 points at 3m-FU, and 7.1 points at 12m-FU with significantly lower values over time (see Table 1). Values for the control half at corresponding time points were significantly higher (see Table 1). On the observer scale, values from the verum half were better (lower), and significant differences favouring the verum half were found for all monitoring times. Table 2 presents the acquired values.

LASCA was carried out in all three phases and the values acquired were expressed as perfusion units (PU). While experimental sites reached on average 115 PU at EOT, the average was 69.8 PU at 3m-FU and 50.2 PU at 12m-FU. Control sites displayed significant higher values of vascularity (122.2 PU at EOT, 73.9 PU at the 3m-FU, and 52.2 PU at the 12m-FU). In all three phases, results for experimental sites were significantly better than control sites. Table 3 presents all the mean values from LASCA for patients in the set.

Significant differences were found in the values for R0, R1, R3, R4, R5, R6, R8, F0, F1, and Q0, with sites treated with Oleogel-S10 displaying more favourable values. The mean R0 value for sites treated with Oleogel-S10 was 0.079 while the mean for control sites was only 0.063 ($p<0.001$). R8 (or Ua) had similar results with a mean of 0.074 for treated sites and 0.059 for control sites ($p<0.001$). Table 4 states all measured values.

DISCUSSION

The search for high-quality wound dressings and topical products has led to a great number of different dressings, which are used today in wound management of wounds including donor site wounds. The optimal dressing or topical product should ensure a proper environment for supporting epithelialization, prevent multiplication of potentially pathogenic microorganisms and thereby the development of infectious complications at the donor site area, to minimize patient's pain and discomfort during changes of dressing, to ensure a favourable final cosmetic effect, and, last but not least, be easy to handle and not too expensive.[9]

Oleogel-S10, the ointment used in this study, is a new product with the clear ambition to come closer to the ideal for a wound topical product.[10] It is a betulin-rich triterpene dry extract from birch bark. The potential of triterpenes to accelerate wound healing has been frequently mentioned recently.[11] Triterpenes, such as betulin, lupeol, and betulinic acid, represent a promising group of natural substances with interesting potential to support keratinocyte division and may thus accelerate wound healing and support epithelialization.[12] The extract is acquired from birch cork (the outer layer of bark). Oleogel-S10 contains sunflower oil and birch bark extract (10%). Birch bark contains in particular lupeol (0.4–4%), erythrodiol (0.5–2%), betulin (60–95%), betulinic acid (0.5–6%), and many other substances.[13] Oleogel-S10 has been designated by the European Commission as an orphan medicinal product for the treatment of the hereditary skin disorder Epidermolysis bullosa. Another area for its use is as part of therapy for actinic

n=30	Verum[a]	Control[a]	Difference[a]	p[b]
Patient:				
EOT	12.1 ± 3.1	14.6 ± 3.0	2.5 ± 2.2	**<0.001**
3m-FU	9.0 ± 1.8	10.2 ± 2.1	1.2 ± 1.1	**<0.001**
p[c]	<0.001	<0.001		
12m-FU	7.1 ± 1.2	7.6 ± 1.1	0.5 ± 0.9	**0.007**
p[c]	<0.001	<0.001		
Observer:				
EOT	14.2 ± 2.8	16.7 ± 2.7	2.5 ± 2.4	**<0.001**
3m-FU	10.6 ± 2.0	11.7 ± 2.6	1.1 ± 1.6	0.003
p[c]	<0.001	<0.001		
12m-FU	8.2 ± 1.1	8.5 ± 1.1	0.3 ± 0.8	**0.046**
p[c]	<0.001	<0.001		

Table 2. POSAS – comparing effects of verum and control at various times on patient and observer scales

[a]Mean and standard deviation.

[b]p-value for Wilcoxon paired test.

[c]p-value for Wilcoxon paired test to compare values at EOT with those at 3m-FU and 12m-FU.

n = 30	Verum[a]	Control[a]	Differences[a]	p[b]
EOT	115.0 ± 34.4	122.2 ± 36.1	7.1 ± 9.4	**<0.001**
3m-FU p[c]	69.8 ± 15.9 <0.001	73.9 ± 18.7 <0.001	4.1 ± 7.3	**<0.001**
12m-FU p[c]	50.2 ± 12.6 <0.001	52.2 ± 13.0 <0.001	2.0 ± 5.2	**0.016**

Table 3. LASCA – comparing effects of verum and control at various times (perfusion unit)
[a] Mean and standard deviation.
[b]p-value for Wilcoxon paired test.
[c]p-value for Wilcoxon paired test to compare values at EOT with those at 3m-FU and 12m-FU.

Parameter	Verum[a]	Control[a]	Difference[a]	*p*[b]
R0	0.079 ± 0.031	0.063 ± 0.029	−0.016 ± 0.016	**<0.001**
R1	0.005 ± 0.003	0.004 ± 0.003	−0.001 ± 0.002	**0.020**
R2	0.938 ± 0.037	0.938 ± 0.031	−0.001 ± 0.024	0.572
R3	0.085 ± 0.033	0.069 ± 0.030	−0.016 ± 0.017	**<0.001**
R4	0.008 ± 0.007	0.006 ± 0.005	−0.002 ± 0.004	**0.010**
R5	1.234 ± 0.496	1.330 ± 0.506	0.096 ± 0.449	**0.028**
R6	0.810 ± 0.462	0.974 ± 0.507	0.164 ± 0.505	**0.002**
R7	0.666 ± 0.151	0.659 ± 0.132	−0.008 ± 0.075	0.428
R8	0.074 ± 0.031	0.059 ± 0.027	−0.015 ± 0.016	**<0.001**
R9	0.006 ± 0.002	0.006 ± 0.002	0.000 ± 0.002	0.811
F0	0.014 ± 0.004	0.013 ± 0.004	−0.001 ± 0.002	**0.005**
F1	0.009 ± 0.005	0.008 ± 0.004	−0.002 ± 0.003	**0.007**
F2	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	–
F3	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	–
F4	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	–
Q0	15.728 ± 6.297	12.592 ± 5.710	−3.136 ± 3.300	**<0.001**
Q1	0.874 ± 0.055	0.872 ± 0.047	−0.003 ± 0.030	0.453
Q2	0.816 ± 0.089	0.816 ± 0.078	0.000 ± 0.046	0.910
Q3	0.058 ± 0.037	0.056 ± 0.035	−0.003 ± 0.022	0.766

Table 4. Viscoelastic parameters with Oleogel – verum vs. control
[a]Mean and standard deviation.
[b]p-value for Wilcoxon paired test.

keratosis.[14,15] Oleogel-S10 is currently being studied very intensively in terms of its effect not only on healing donor sites but also on healing burns themselves.[12] One of the important differences between these two types of skin wounds is in their homogeneity. No burn has ever the same depth across its entire extent and so various healing times can be expected for different parts of a wound. In contrast, donor sites are far more homogenous, and this simplifies randomization as well as monitoring of the course of healing because there is no effect of different wound depths.

Our results clearly indicate accelerated healing at donor sites treated with Oleogel-S10 in comparison to control sites. Although the difference between the groups was relatively small, it may have relevant impact for difficult to heal wounds. In general, donor sites are standardised wounds without disturbing factors. Similar to our study, other studies have also reported only small differences in time to heal. The small difference in healing related to a significant improvement in scar quality. With the use of objective methods such as LASCA and the Cutometer MPA580 we also demonstrated that the wound half treated with Oleogel-S10 has shown significantly better rheological and functional (viscoelastic) results. The Cutometer provides one of the most widely used methods for objectively determining viscoelastic skin parameters.[8] In our patient set, we always evaluated two defined points for each site half. Individual measurements were conducted 12 times in total at each point, and the resulting values were averaged. With the use of the Cutometer, the vertical deformation of skin is measured as the skin is drawn into the probe. Significant differences were found in the values for R0, R1, R3, R4, R5, R6, R8, F0, F1, and Q0, with sites treated with Oleogel-S10 displaying more favourable values. The most important parameter, R0, corresponds to the first maximal amplitude or final deformation. This parameter represents the passive behaviour of skin to force (firmness). R0 on the half treated with Oleogel-S10 was 0.079 ± 0.031 and on the control half 0.063 ± 0.029 ($p < 0.001$). The R0 results unambiguously indicate that experimental sites had greater ability to achieve maximum amplitude. Another important R parameter is R8 (Ua), redeformation ability. For examined sites, R8 was 0.074 ± 0.031 and for control sites 0.059 ± 0.027 ($p < 0.001$). These values indicate that the redeformation ability (i.e. the ability to return to the original state) was greater for the wound half treated with Oleogel-S10.

POSAS is currently one of the most universal scales for assessing scars' character and changes over time.[16] In comparison to other scar scales it has a linear scale and allows proper calculation.[17] The assessment includes two scales, the patient's and the observer's scale. We used POSAS for assessment three times during the study, first at wound healing (i.e. at EOT) and then at 3m-FU and 12m-FU. As expected the acquired results indicate that over the monitored period values improved not only at experimental sites but also at control sites. This underscores the necessity for any anti-scarring strategy to include a control group. Values from within-subject comparison were significantly higher at all monitoring times from the half treated with Oleogel-S10, clearly indicating the benefit of the drug. The acquired results correlate very closely with objective measurements and data acquired from LASCA and the Cutometer MPA 580.

In general, the ointment was well tolerated and no allergic reaction was recorded. Across the entire clinical study, only one adverse event was recorded. This event was the development of infectious complications, which had originated in the control half, but the potentially pathogenic microorganism spread over 5 days to the already epithelialized site treated with Oleogel-S10. This complication required antibiotic therapy. The infectious agent was identified as *Staphylococcus aureus*. It can nevertheless be assumed that support for keratinocyte differentiation alone would have had an antimicrobial effect. Moreover, studies have unambiguously confirmed that certain triterpenes inhibit the growth of potentially pathogenic micro-organisms.[18] Awolola et al. had examined the antibacterial effects of three triterpenes and three flavonoids against a number of bacteria – *S. aureus* and *Escherichia coli*.[19] In particular, the activity of lupeol acetate against *S. aureus* strains was observed to be very promising. Antibacterial as well as antifungal effects had been determined by Mutai et al. in triterpenes acquired from extracts from the stem bark of *Acacia mellifera*.[20] That study again tested against *S. aureus* strains, as well as *Microsporum gypseum* and *Trichophyton mentagrophytes*.

CONCLUSION

The acquired results clearly demonstrate the effectiveness of using Oleogel-S10 to accelerate donor site epithelialization. This acceleration is accompanied not only by reduced wound healing time but also the creation of much higher-quality skin with viscoelastic parameters comparable to those of intact skin. We must also conclude that this product was completely safe across the entire clinical study, and despite the single infectious complication, no undesirable side effects were recorded.

Other clinical trials using Oleogel-S10 in patients with acute non-thermal skin loss (epidermolysis bullosa, toxic epidermal necrolysis, etc.) are now at different stages of progression.

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THE NASOLABIAL FLAP: THE MOST VERSATILE METHOD IN FACIAL RECONSTRUCTION

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SUMMARY

The nasolabial flap was described 170 years ago and still remains one of the most frequently used methods in facial reconstruction. This technically easy and maximally effective procedure has become a real workhorse and an integral instrument for every plastic surgeon. Over time multiple modifications of this technique have been described. In this article, authors present an overview of nasolabial flap modalities and discuss advantages and disadvantages of these techniques.

KEYWORDS

flap, nasal defect, nasolabial flap, nose reconstruction

INTRODUCTION

The nasolabial (also called melolabial) flap was one of the first local flaps used for closure of defects in the midfacial area. It was described in 1846 by a German surgeon, Johann Friedrich Dieffenbach, and still remains the most useful option for reconstruction in the area of facial triangle due to its versatility and effectiveness.[1, 2] Over 560 articles were found in PubMed search for nasolabial flap between 1960 and 2016.[3]

This flap may be either superiorly or inferiorly based. The most commonly used superiorly based flap is useful for defects of the central and lateral nasal dorsum as well as the nasal tip and ala. This technique allows harvesting a huge flap along the whole length of nasolabial fold down to the border of the chin and in the width determined by the amount of natural excess of tissue at the nasolabial crease and its extensibility. The inferiorly based flap is useful for upper and lower lip defects, the floor of the nose and reconstruction of the columella.[4, 5] (Fig. 1, 2.)

ANATOMY OF THE VASCULAR SUPPLY

The paranasal cheek area is supplied medially by the angular artery and its perforating branches. The central cheek is supplied by the perforating branches from the internal maxillary artery as well as by extensions of the transverse facial branch from the superficial temporal artery. The nasolabial flap can be used as a random pattern type or it can be lifted as an axial pattern flap. The vascular supply to random flaps arises from the subdermal vascular plexus and dermal

Fig. 1. Nasolabial flap with superior pedicle

Fig. 2. Nasolabial flap with inferior pedicle

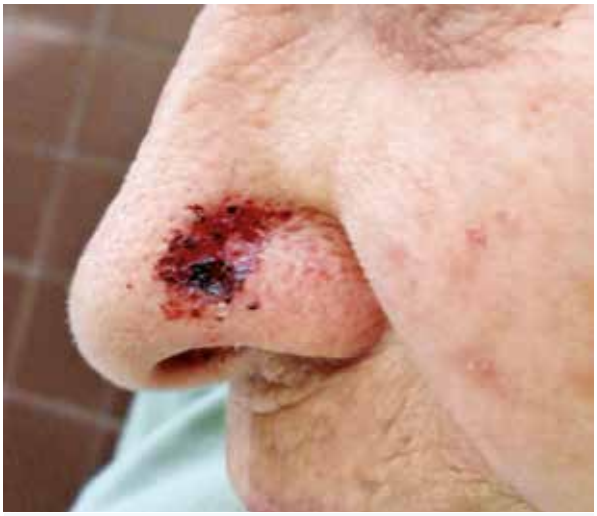

Fig. 3. Tumorous infiltration of the nasal ala

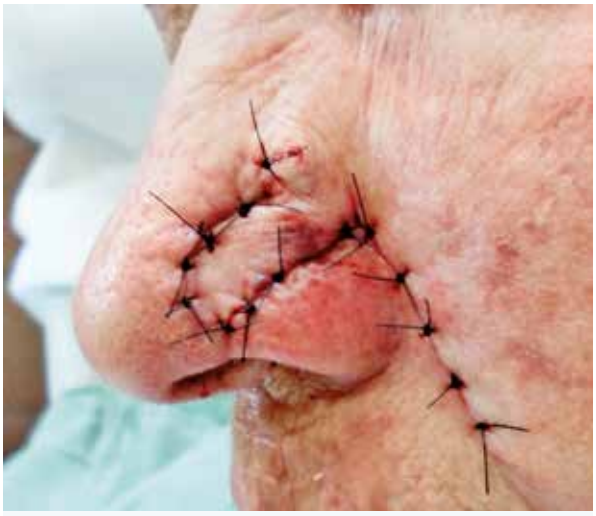

Fig. 4. Transposition nasolabial flap

plexus, which are ultimately supplied by musculocutaneous arteries. Thus, the appropriate plane of dissection is subcutaneous fat. [6]

NASOLABIAL FLAP MODALITIES

Transposition flap

This technique, usually based on the superior pedicle, allows the use of the cheek tissue adjacent to the upper lip from which a larger flap can be harvested. The flap is raised and transferred as a single stage procedure to an immediately adjacent defect. With the paramedian forehead flap, this technique is the most suitable method for reconstruction of the nasal lobule.

When the defect is on the lateral nasal lobule and does not cross the midline, the flap may be based only on dermal blood supply.

The medial border of the flap should be drawn from the tangent at the edge of the defect so as to leave the lateral alar crease intact. The flap is then back-cut to approximately the same level and a Burrow´s triangle is removed from the upper lateral nasal skin. The cheek skin over the malar and buccal areas is then elevated in a subcutaneous plane, so that the transposition flap becomes a secondary extension from the edge of the cheek advancement flap. The nasolabial transposition flap should be defatted to the appropriate thickness at the time of transfer so that a secondary revision should be unnecessary. The flap could also be folded upon itself for nasal lining or extended past the midline. In this case, consideration may be given either to delay the flap or to maintain a direct communication with the subcutaneous portion of the pedicle and its branches from the angular artery.[6, 7] (Fig. 3, 4.)

Transposition nasolabial flaps are very often used for reconstruction of complex nasal defects especially in the alar and tip regions. The flap could be folded upon itself to restore nasal lining usually in combination with other flaps such as forehead or contralateral nasolabial flaps.[8, 9, 17, 24] (Fig. 5.)

Interpolation flap

Interpolation flaps are similar to transposition flaps with the difference that the interpolation flap is lifted over an area of normal skin to reach the defect. The base of the flap is not immediately adjacent to the recipient site. This arrangement results in a bridge of tissue, or pedicle, between the flap base and the surgical defect. These flaps are used when insufficient tissue or mobility in nearby skin prevents coverage of a surgical defect with primary closure or an adjacent flap. An interpolation flap is a two-stage surgery. The bridge must be disconnected in a second stage when the new vascular supply is established between the wound and the flap (usually after 3 weeks).[7, 10, 11] (Fig. 6 A–D.)

This method is very suitable for nasal tip or columella reconstruction. Often in combination with cartilaginous grafts, mucosal flaps or skin grafts, it could be used for rconstruction of penetrating (complex) nasal defects.[10, 11] (Fig. 7A–D.)

Advancement flap – V-Y flap

A sliding flap from the nasolabial fold in a V-Y manner is well suited for reconstructing the area where the lower or middle third of the nose meets the cheek. Like the island flap, the sliding flap is generally slid into the defect on a subcutaneous pedicle.[7, 12] (Fig. 8A–D.)

Subcutaneously pedicled island flap

This method popularized by Bouisson (1864) is also useful for reconstructing small defects in the nasal flank area. The flap may be based on the facial artery or be designed with a subcutaneous pedicle that has an inferolateral or superolateral position in relation to the flap. The skin between the flap and the defect is undermined, and the pedicle is pulled through. Care is taken not to place excessive torsion or pressure on the flap pedicle. Because the subcutaneous pedicle often creates fullness at the pull-through site, this is not one of the most favourite flaps. The cheek must be mobilized somewhat more widely than with other flaps to avoid distorting the upper lip.[4, 6, 7, 13]

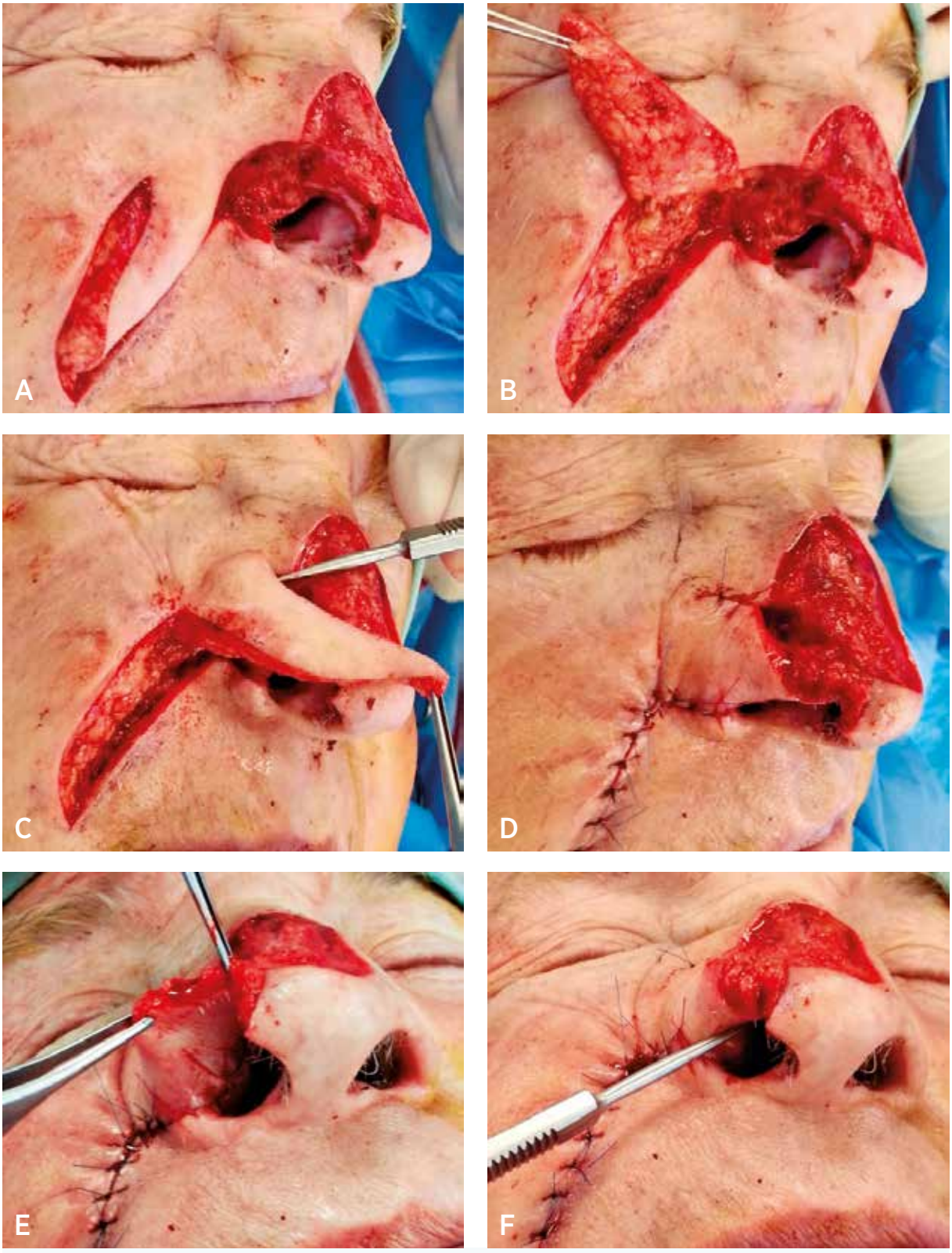

Fig. 5A–F. Sequence of nasal lining reconstruction with transposition nasolabial flap

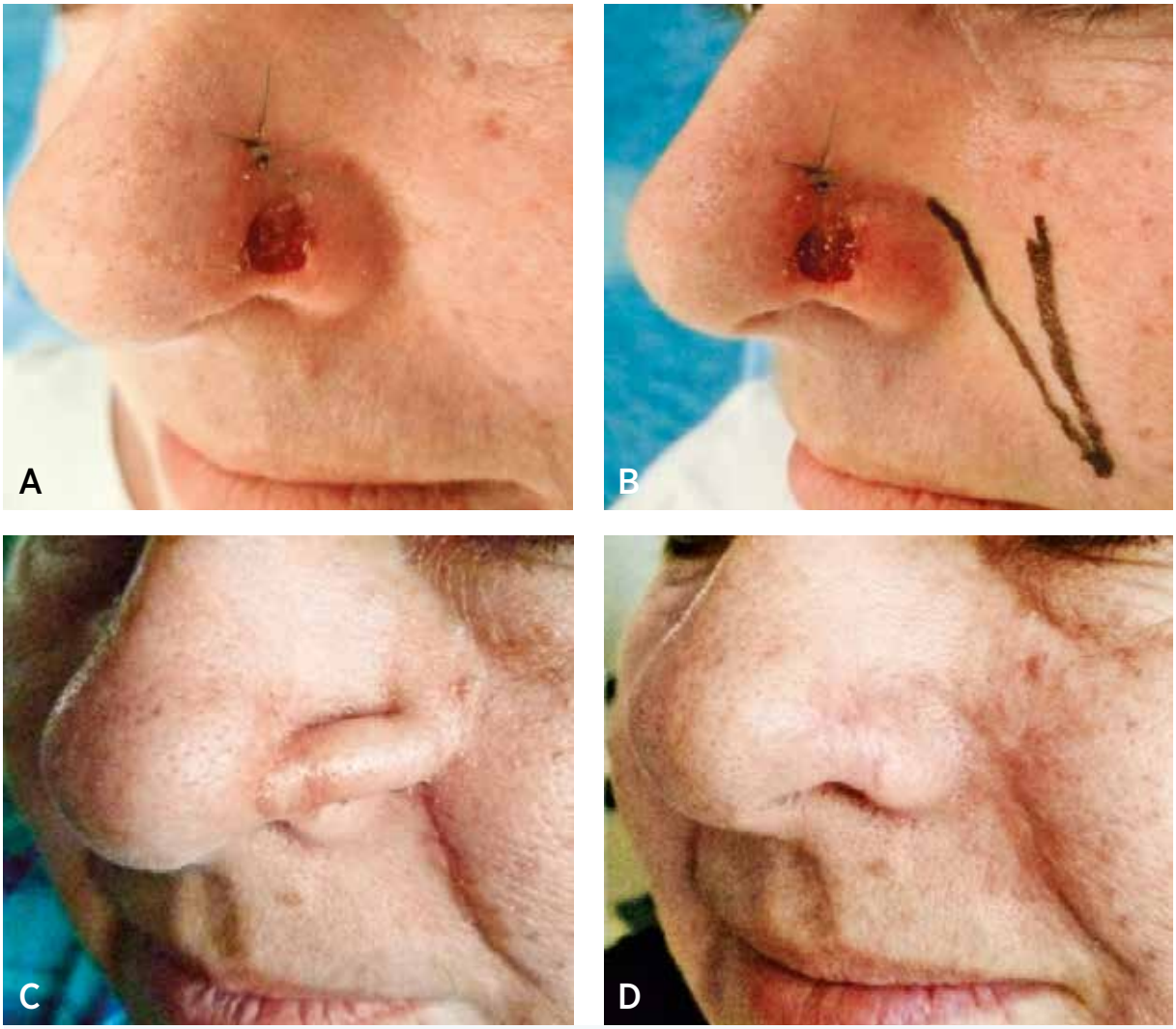

Fig. 6A–D. Sequence of nasal ala defect reconstruction with interpolation nasolabial flap

Facial artery perforator based nasolabial flap

The facial artery perforator-based nasolabial flap is supported by the study of angiosomes of the facial region and is usually based on the superior labial artery perforator, including the facial artery perforator. These flaps are designed as rotation propeller flaps. The term "propeller flap" is an island flap that reaches the recipient site by axial rotation. This technique allows greater freedom in rotation, mobility, and flap design for the reconstruction of perinasal defects. Possible negative aspect of this method is the time required. Perforator dissection is a more difficult procedure than the use of other local flaps that do not require perforator dissection.[14, 15]

Nasolabial free flap

A nasolabial free flap consisting of a part of the risorius and buccinator muscles, buccal mucosa, and nasolabial skin is rarely used for reconstruction of full-thickness lower eyelid defects. This flap, supported by the facial vessels, is transported via microvascular anastomosis to the superficial temporal vessels.[16]

DISCUSSION

When choosing the method of facial reconstruction, it is necessary to carefully consider surgical stress on the patient, the technical demand of the approach, and the type of anaesthesia. These circumstances must meet the expected benefit of the surgery. The surgery must be undergone in a disease free terrain, however, it is necessary to maintain good function and an acceptable appearance. The need of functional and aesthetic effects may be different according to each individual personality. The simplest method for closure of facial defects is a skin graft. It can be used only in superficial defects with a suitable vascular bed.[11, 21, 22]

The cosmetic outcome of skin grafts may be poor due to the colour and texture mismatch. Especially in nasal reconstruction, local flaps such as nasolabial or dorsal nasal flap have better results. Bilobed flaps are now largely abandoned in nasal reconstruction because they almost violate the subunit principle either at the donor site or

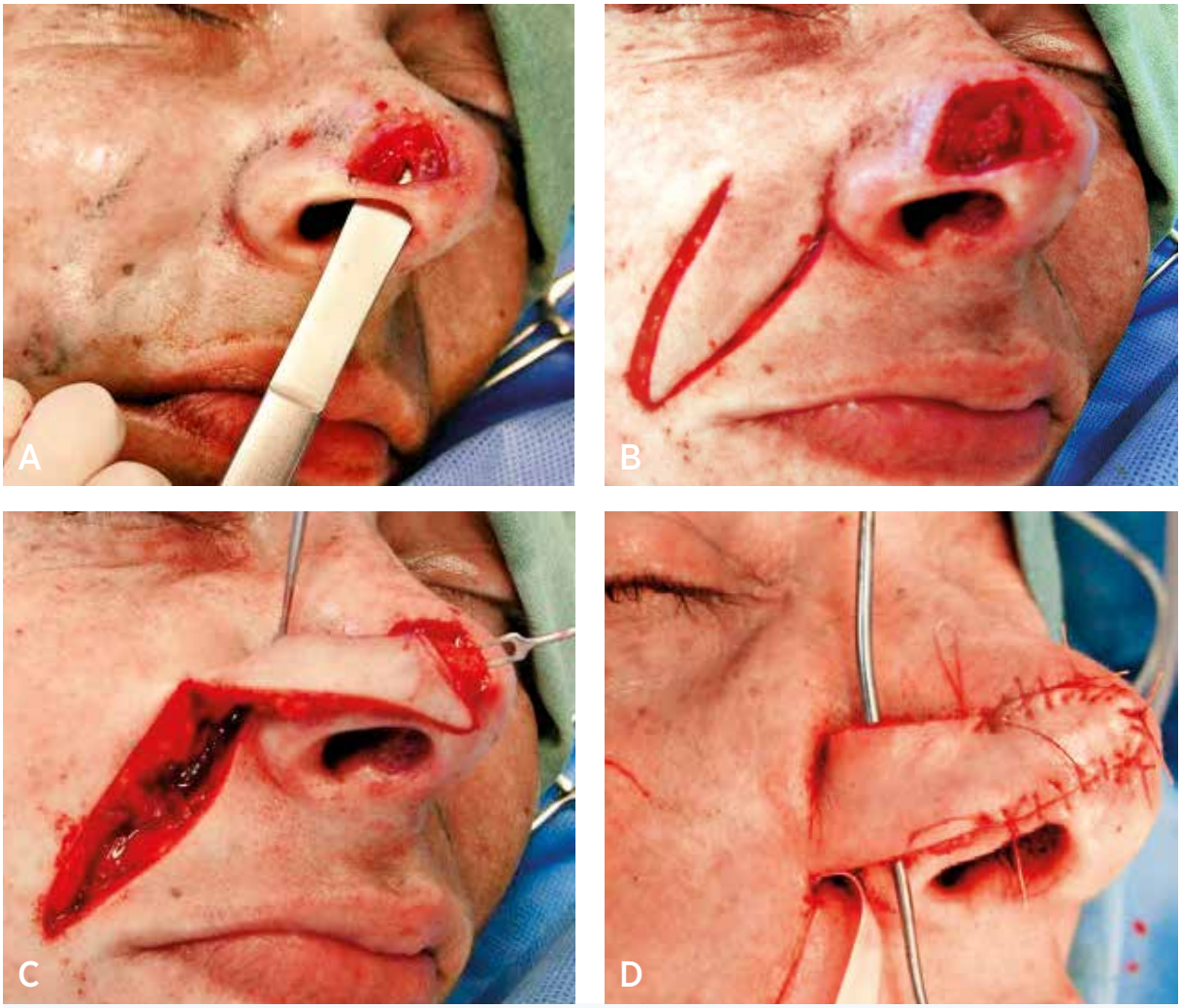

Fig. 7A–D. Sequence of reconstruction of a penetrating defect of the nasal tip with interpolation nasolabial flap in combination with nasal mucosal advancement

at the recipient site.[19] Dorsal nasal flaps are often linked with apparent scars and are insufficient for large tip defects.[1]

In deep and large defects of the nose and the centrofacial region, only nasolabial and forehead flaps can be used. The forehead flap, which is more suitable for larger defects of the nasal dorsum and tip, represents more encumbering two-stage surgery, which requires general anaesthesia and results in a more visible scar at the donor area[18]. Postoperative morbidity can be considerably higher for forehead flaps than for nasolabial flaps.[1, 18, 19, 23, 25]

The nasolabial flap perfectly matches the requirements of complex reconstruction of small and middle size defects including the possibility to combine it with a cartilage graft or a contralateral flap. Technically, it is an easy surgery performed in local anaesthesia with minimal donor site morbidity. Disadvantages of this procedure are the risk of transferring hairy skin onto the nose and two-stage procedure in the interpolation variant of this flap.[20, 21, 22, 23, 25]

CONCLUSION

The nasolabial flap is an easy, quick and effective approach for treatment of smaller and middle-sized defects of the midfacial area. This technique allows harvesting a wide and rich vascularized flap along the whole length of the nasolabial fold. In combination with the wide arc of rotation, the flap could reach almost any site of centrofacial area. The flap perfectly matches the requirements of complex reconstruction including the possibility to combine it with cartilage graft. It produces a good functional and aesthetic outcome with minimal donor site morbidity and overall stress for the patient. Therefore, it is suitable for patients with higher expectations even in cases that they are old and polymorbid. Due to its versatility and effectiveness, the nasolabial flap still remains the most useful option for reconstruction in the area of facial triangle.

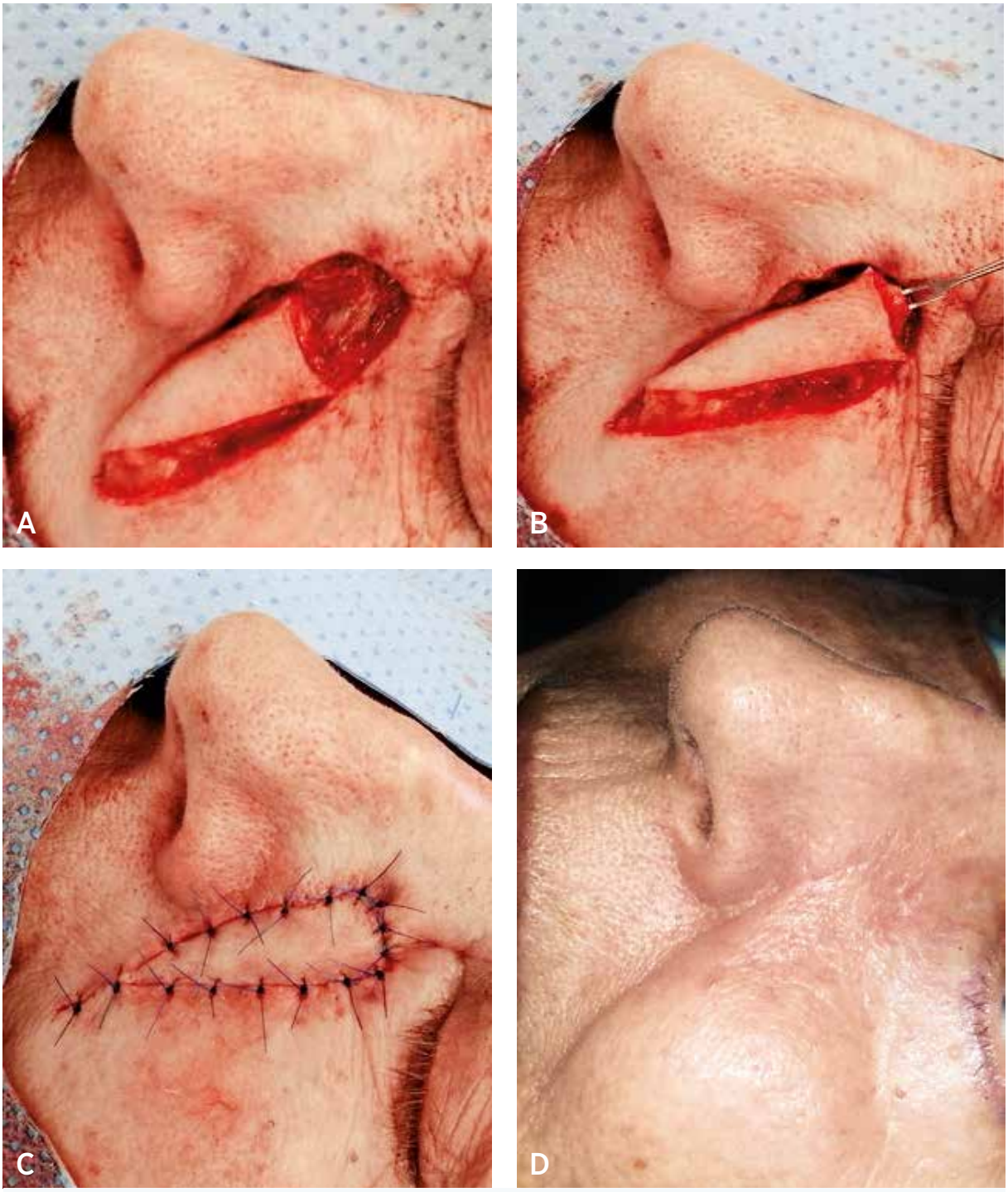

Fig. 8A–D. Sequence of reconstruction of defect on the nasal-cheek border with V-Y advancement nasolabial flap

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CURRENT TREATMENT OPTIONS OF DUPUYTREN´S DISEASE

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SUMMARY

Dupuytren's disease (fibromatosis of the palmar fascia, benign neoplastic fibromatosis, Dupuytren's contracture) is a disease characterized by growth and successive contracture of single parts of the palmar aponeurosis. This condition is known and has been treated for several centuries. In the advanced stages of the disease, it leads to significant limitation of hand function, resulting in reduced quality of life of the patient. Dupuytren's disease (DD) is a life-long disease with a variable course and a heterogeneous clinical presentation. Therapy focuses on the clinical manifestations of the disease as well as on reduction of the functional limitation of the hand caused by the disease. In addition to conservative and surgical procedures, there are also some mini-invasive methods available. Treatment should be reserved for centres and experienced surgeons specialized in hand surgery.

KEYWORDS

Dupuytren's disease, Dupuytren's contracture, surgical treatment, clostridium collagenase, collagenase of *Clostridium histolyticum*, palmar fasciotomy, palmar fasciectomy

INTRODUCTION

One of the first to describe this disease was Felix Plater in 1614. The current opinion that Plater considered the pathological basis of disease to be a contracture of the flexor tendons is a misinterpretation of the original Latin text. Plater's anatomical studies demonstrated that shortening of ligamentous palmar aponeurosis is the anatomical basis responsible for DD.[1] During the eighteenth century, DD was also studied by Henry Cline (1777) and his student Astley Cooper, who reported in detail about DD in 1822 in his publication "A Treatise on Dislocations and Fractures of the Joints".[2] A Parisian surgeon, Baron Guillaume Dupuytren (1777–1835), is known as the father of treatment of the disease. He did not publish any comprehensive monograph, but since 1831 he lectured about DD for his colleagues and students and they kept his name associated with the disease through oral transcripts called Leçons orales and gave the disease its current name. It is known that Dupuytren himself did not like to write.[3,4]

DD occurs predominantly in males with a ratio varying from 2:1 to 10:1.[5] The differences observed in male prevalence can be however attributed to the fact that women have more often milder forms without functionally significant flexion contractures and slower progression of DD. So some of the affected women may not be enrolled to the prevalence studies in operated patients.[4] Most cases are observed in the 6th decade of life. The disease affects primarily the white race. The highest prevalence is reported in the Nordic countries and in the countries where civilization expansion from these countries occurred. Therefore, DD is sometimes called a Viking's disease. However, by refining epidemiological studies on DD, it seems that this correlation is likely to be significantly lower. The worldwide prevalence of DD varies greatly from 0.6% to 31.6% (depending on the classification criteria; a large number of patients with mild stages of the disease do not visit doctors and the disease then appears more rare than it actually is). The origin of the disease is probably multifactorial with a significant genetic component. In patients with a positive family history is the manifestation of the disease in average 5 years earlier than in those without positive family history.[6] Other major risk factors include civilization diseases, especially diabetes mellitus, abuse of alcohol, side effect of some antiepileptic drugs in patients with epilepsia and smoking. We cannot simply say that these diseases themselves are the cause of DD. It only appears to be more common in patients with DD than in the general population. The effect of heavy manual work itself has not been recently considered to be an aetiological factor. On the other hand, small non-penetrating injuries or long-term exposure to vibrations are considered to contribute on the development and progression of DD.[7]

The palmar aponeurosis begins at the distal edge of the transverse carpal ligament and its projections continue into septa and skin of midpalmar space and on the fingers. In the mid-palmar space, it merges with the palmar fascia,

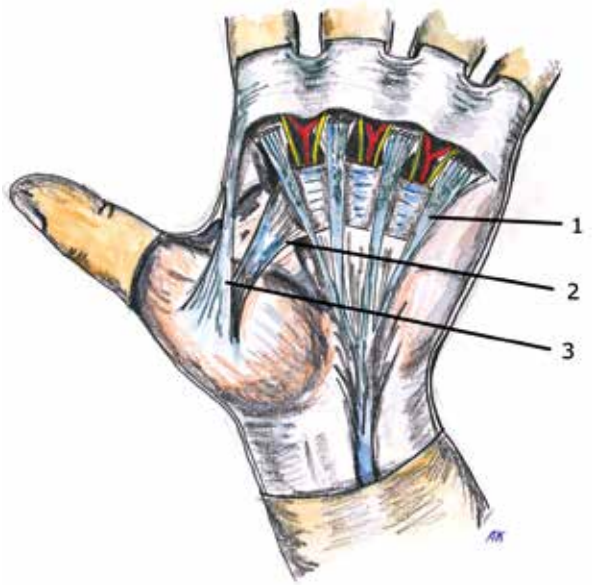

Fig. 1. Anatomy of palmar aponeurosis
1. Longitudinal pretendinous fibers
2. Proximal commisural ligament of 1st web space
3. Distal commisural ligament of 1st web space

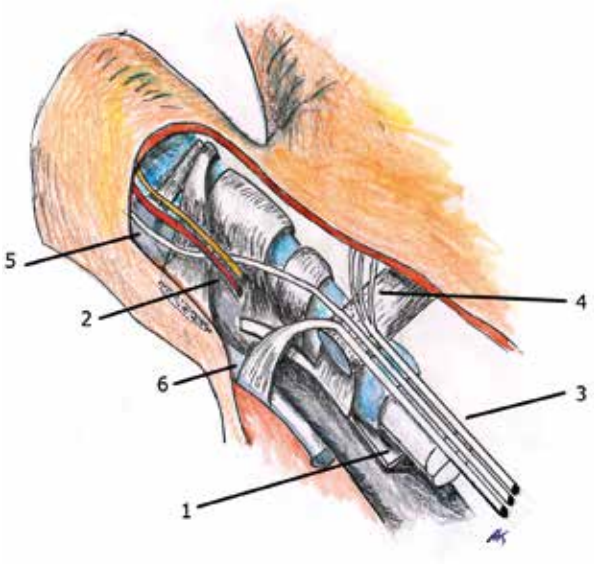

Fig. 2. Anatomy of pretendinous fibers in the area of its transition to the fingers
1. Flexor tendons
2. Neurovascular bundle
3. Pretendinous fibres
4. Superficial fibers
5. Intermediary fibers
6. Deep fibers (an its course to dorsal extensor aponeurosis)

then it inserts in the radial and ulnar aspect into thenar and hypothenar fascia. The tendon of palmaris longus muscle inserts into the palmar aponeurosis at the distal edge of the transverse carpal ligament and stretches the aponeurosis by exerting tension on it (this occurs mainly in cats). In the area above the tendons of the 2nd to the 5th finger, the palmar aponeurosis creates individual longitudinal bands, which are distributed distally in the palm into three portions – superficial, intermediate and deep fibers. The superficial fibers are attached into the skin near the MCP joints, the middle fibers are attached into the natatory ligaments (ligamentum metacarpale transversum superficiale) and finger fascia (they are called spiral fibers) and deep fibers into the area of the MCP joints and it goes deeply and attaches close to extensor aponeurosis. In the area of the fingers is the course of the fibers a little bit more complicated. The finger fascia is based on Grayson's prevascular and Cleland's retrovascular ligaments that extend into the lateral digital fascia, which continues as a portion of the fibers from the natatory ligaments and from the spiral fibers from the pretendious bands (Fig. 1, 2, 3).

In case of pathologically affected aponeurosis the individual bands are transformed into thickened and rigid cords. The initial stages of the disease can be manifested by the formation of palmar skin pits, subcutaneous nodules and the contraction of the cords. In the area of the palmar fascia the pathologically modified cords cause a gradual contraction in MCP joints. If the fingers are also affected, there is a gradual pathological transformation of the individual parts of the digital fascia. In this area they gradually form three main structures that cause contracture of the PIP joint.[8] The first one, the central cord, is a continuation of the pretendinous cord that is attached to the flexor sheath and periosteum of the middle phalanx. Furthermore, a lateral cord can

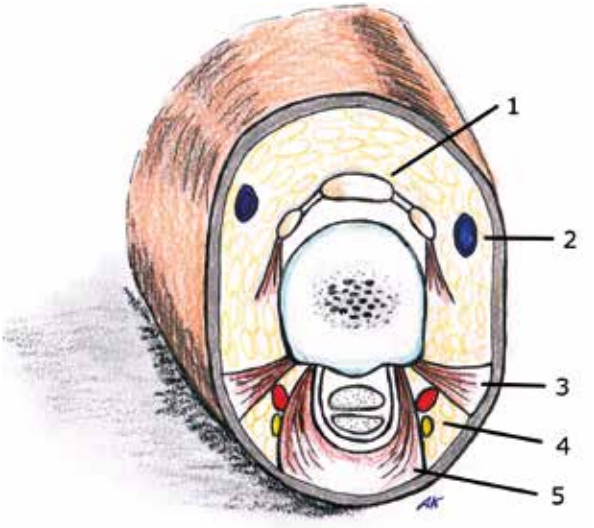

Fig. 3. Anatomy of ligaments in the fingers
1. Extensor tendon
2. Dorsal vein
3. Cleland's retrovascular ligament
4. Neurovascular bundle
5. Grayson's prevascular ligament

be formed by transformation of the lateral digital sheath, which can also cause contracture of the DIP joint. A relatively complicated structure is the so-called McFarlan's spiral cord.

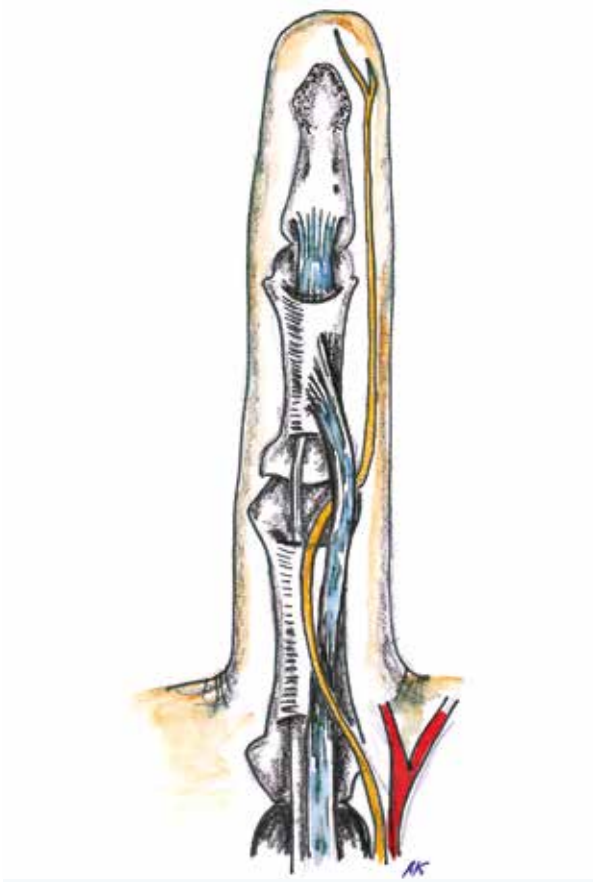

Fig. 4. McFarlan's spiral cord

It is caused by the transformation of the spiral fibers, fibers of the natatory ligaments, parts of the Grayson's ligaments and lateral digital sheath. It causes flexion contracture at the PIP joint and its course deviates the neurovascular (NV) bundle medially and superficially (Fig. 4).

Histopathologically the composition of a healthy and affected palmar aponeurosis is different. While the normal aponeurosis consists predominantly of collagen I (90%) and partially of collagen III (5%), the affected aponeurosis contains up to 40% of collagen III and numerous fibroblasts and myofibroblasts. One of the theories of the pathophysiological basis of the disease is based on the effect of oxygen radicals. It's production is a reaction to local ischemia or high concentration of alcohol.[9] Increased formation of oxygen radicals was indirectly demonstrated by higher concentrations of substances that catalyze their formation in pathological tissue.[10] Environment with a high concentration of oxygen radicals further causes production of growth factors (BFGF, PDGF, TGF-β) that stimulate proliferation and subsequent contracture of myofibroblasts.

A simple classification according to Karfík is used historically. It classifies the clinical forms into 3 stages. This type of classification considers the extent and location of the pathological process: type 1 – palmar form (without finger contracture), type 2 – simple contracture, type 3 – complicated contracture. In the case of simple contracture, we can observe flexion contractures of MP and PIP joints, most often on the 4th and 5th fingers. The complicated type of contracture is manifested by the impairment of the whole ligamentous system of the palm itself . Contractures of several or all fingers, adduction contracture of the thumb and severe impairment of the aponeurosis and palmar skin are typical. The palm can have a cuplike appearance.[3,8]

Stages of DD	according to Iselin
I. stage	nodes in the palm
II. stage	nodes in the palm, semiflexion of MPJ
III. stage	nodes in the palm, semiflexion of MPJ and PIPJ
IV. Stage	nodes in the palm, semiflexion of MPJ, PIPJ, hyperextension of DIPJ

Table 1. Stages of DD according to Iselin

Stages of DD	acccording to Mikkelson
I. stage	nodes and cords without contracture
II. Stage	contracture 1–45°
III. Stage	contracture 45–90°
IV. Stage	contracture 90–135°
V. Stage	contracture over 135°

Table 2. Stages of DD according to Mikkelson

Classification of DD according to Tubiana	
Phase	Description
0	Physiological finding
N	Palmar or digital node, without developed flexion contracture
1	extension deficit 0–45°
2	extension deficit 45–90°
3	extension deficit 90–135°
4	extension deficit over 135°

Table 3. Classification of DD according to Tubiana

Another known, simple and used classification is the Iselin system. He has divided DD into 4 stages according to the location of the disease; see table (Table 1). Better knowledge of the stage of contracture is provided by the classification according to Mikkelson. The various stages of the disease are assigned a degree of contracture (Table 2). Complex evaluation of DD is provided by Tubiana classification (Table 3). It considers the localization of the disease (including both two and three phalanx fingers), the degree of contracture and the impairment of the webspaces.[8] Generally, the best classification is such one that provides instructions for treatment of DD. From this perspective, we can be satisfied particularly with Tubiana classification and with Mikkelson classification.

TREATMENT OF DUPUYTREN´S DISEASE

In patients with functional disability of the hand due to DD the fastest and most radical removal of the affected

tissue is not the main objective – unlike in cancer patients. The most important for the correct treatment of DD is currently, in addition to proper timing, also the choice of the most optimal steps that ensures the maximal function of the affected hand with minimal morbidity and minimal risk for the patient. Radical and apparently the most effective therapy of DD is the classical surgical treatment that, however, causes considerable morbidity.[8] The decision about the suitable surgical technique should be based on the local finding as well as other factors such as social history, occupational history, age and mental status of the patient.

Conservative treatment

Conservative treatment of DD includes or in the past included radiotherapy, splinting, massages, topical use of vitamin E ointments, steroid injections, ultrasound, shockwave and laser therapy. The relatively new treatment option, which has changed the DD treatment algorithm in recent years, is the use of Clostridium histolyticum enzyme (enzymatic fasciotomy). It is not classified as a conservative treatment but rather as a separate group of so-called mini-invasive procedures. Conservative treatment has its place as a surgical therapy or a method to slow the progression in early stages of the disease. Physical methods (ultrasound, shock wave, laser, ...) usually lead to softening of the nodes, but in principle they do not affect contracting cords. A good effect is known in the case of long-term use of splinting.[3,7,8,11] However, this is often more restrictive for the patient than the contracture itself. A more effective conservative treatment is the application of steroid injections. They influence the formation of fibrous tissue, whereas they do not affect matured cords, and therefore they are used to treat the nodular form of DD only. The most serious local complication of this treatment is the possibility of spontaneous rupture of the flexor tendon. The exact percentage risk is not known. In addition, up to 50% of the patients usually report only transient atrophy and depigmentation of the skin at the injection site.[12] The efficiency of various conservative procedures is controversial and with little clinical benefit to the patient, conservative treatment is not commonly indicated as first treatment.

Mini-invasive treatment

A relatively new group of therapeutic procedures includes needle aponeurotomy and treatment with Clostridium histolyticum collagenase. Both of these procedures cannot be included simply among surgical procedures or conservative procedures.

Aponeurotomy (some authors also use the synonym fasciotomy) means simple interruption of a contracture cord with immediate release of flexion contracture, followed by patient's rehabilitation. This was the basic technique used by Baron Dupuytren in the 19th century. Aponeurotomy can be performed with small scalpel incisions, but more often it is performed as mini-invasive needle technique (percutaneous needle fasciotomy). Recommended technique includes technique with swinging movements or multiple puncture technique in one spot with a simultaneous passive tension applied with extension of the finger. This interruption is performed several times over the entire contracture cord, and with subsequent manipulation may be achieved full extension of the finger according to the degree and character of the disease. Needle aponeurotomy may be supplemented with lipografting, which, according to the authors, allows shorter recovery and less scarring of the skin by adding fat to the atrophic subcutaneous tissue.[13] But there is not more extensive experience from more independent workplaces in case of this method.

The application of Clostridium histolyticum collagenase (CCH) is also a mini-invasive technique that has already gained its place in addition to the classical aponeurotomy. Clostridium histolyticum collagenase is used under the tradename Xiapex (Auxilium, USA). CCH contains 2 different types of collagenases: collagenase AUX-I (class I) that splits the terminal portions of collagen chains and AUX-II collagenase (class II) that affects the middle parts of the chain. Collagenase should specifically split collagen I and III, especially pathological cords. However, there are other connective tissues of the hand with a similar structure, including the tendons and joint ligaments, which results in a risk of rupture of the flexor tendon as a complication after the procedure. However, this complication is rare when the application guidelines are followed (2 ruptures per 1000 injections are reported in the literature).[14] Other important structures such as vessels and nerves contain predominantly collagen type IV in the walls, which should not be affected by CCH. CCH should always be applied safely to the cord. It is then followed by 1 day of resting or limb fixation with a splint. The next day, the doctor performs manipulation under anesthesia, which breaks the collagenase-infiltrated cords to straighten the finger. Extensions can also be improved by continuous rehabilitation or by stretching or splinting. Regarding the long-term results of CCH treatment, there are currently no sufficient long-term studies available. The results of comparative studies show that the estimated recurrence rate ranges from 10 to 31% over a period of 120 days to 4 years, which is less than in percutaneous needle aponeurotomy (50-58% over 3 to 5 years). In 2010, preliminary results of recurrence in patients enrolled in a phase II trial were published. Follow-up was 8 years. From the original 23 patients, only 8 were followed and examined, so the results cannot be generalized. Results show that CCH treatment can achieve full joint extension in most patients and clostridium collagenase is more effective in treating metacarpophalangeal (MCP) than proximal interphalangeal (PIP) joints. From the 8 patients who were finally checked, 6 had signs of recurrence of the disease, although less than in the previous treatment. None of them underwent surgery, and satisfaction with CCH treatment was high in these patients.[15]

In the study by Peimer et al. (2015), a 5-year recurrence was published after the use of collagenase. The recurrence was defined as an extension deficit of 20 and more degrees in the joint, where the extension deficit achieved by therapy was 0-5 degrees. The total recurrence reported was 47% (for MCP joints 39% and for PIP joints 66%).[16] If we define the recurrence as extension deficit 30 or more degrees, we assume that the resulting recurrence is smaller. Recurrence after fasciectomy varies depending on the criteria for defining recurrences and it is in average around 39%. [17]

Surgical therapy

"The development of experience with surgical therapy follows the development of insight into the basis, the anatomical extent of the disease. From the interruption of the cords, it was correctly concluded that the most effective therapy is removal of affected aponeurosis. Experience with

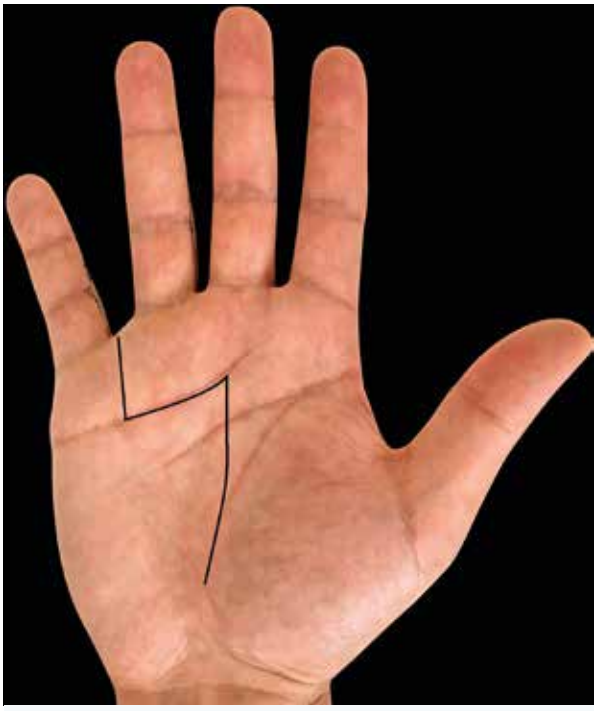

Fig. 5. Incisions according to Meyerding

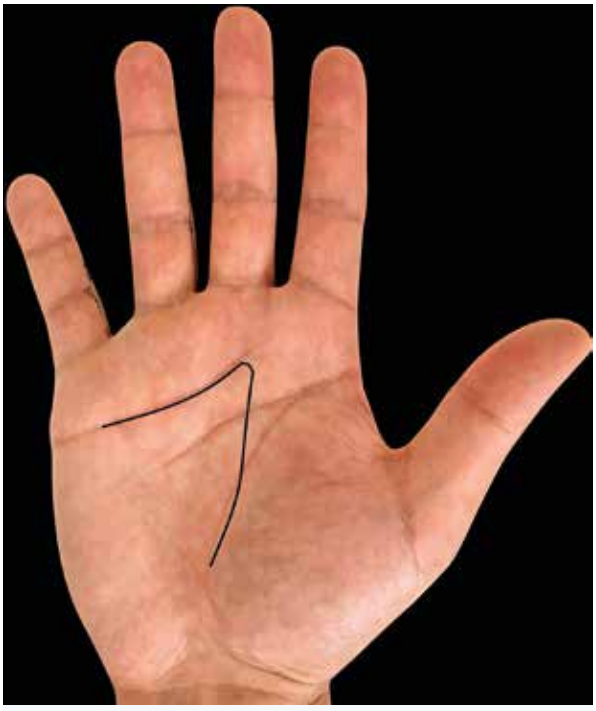

Fig. 6. Incisions according to Burian

recurrences has shown the possibility that the disease develops at any area of palmar aponeurosis and resulted in logical removal of the entire palmar aponeurosis in the palm." [3] This idea of prof. Karfík fully reflects the previous efforts to achieve maximal radicality in removal of pathological palmar aponeurosis. However, when selecting a suitable surgical procedure, it is necessary to consider the clinical findings and overall condition, but also the social background and the patient's needs, considering the expected total duration of treatment and the risk of relapse or recurrence. Radical operations have their indications, but there is no need to perform extensive surgeries with complete removal of unaffected aponeurosis. Secondary morbidity after such an extensive operation is considered to be a greater problem than any other future surgery on other parts of the hand that were not previously affected. General indications of surgical therapy are regular, for example, in a painful palmar form. The most common indication is a contracture in the MCP or PIP joints (30° in MCP or any degree in PIP joint) limiting the patient in everyday life. The commonly used standard for indication of surgical treatment is also the so-called positive "table top test", in which the patient with clinically significant contracture of the finger can not place the palm on a flat tabletop surface.

Together with the choice of the right surgical procedure, we also have to choose the optimal skin incisions so that we could remove maximum of the affected tissue without the need for extensive dissection and at the same time could sufficiently visualize the structures to be protected, such as the tendons, blood vessels and nerves. The most common incisions are shown in Fig. 5, 6, 7. The open surgical procedures for treatment of DD include limited, segmental and radical aponeurectomy or dermofasciectomy.

Limited aponeurectomy (also limited fasciectomy) is currently the most commonly used surgical technique for treatment of DD. This is a procedure with low morbidity. The principle is removal of only pathologically altered tissue in a necessary extent. Any possible skin defects are usually covered by local skin plasties (Z plasty, V-Y plasty), or local skin flaps. Limited aponeurectomy has a significantly lower recurrence rate (20.9% vs. 84.9%) compared with needle aponeurotomy in a 5-year comparison, which is associated with greater patient satisfaction over the long term.[18,19,20] In 1964, McCash published the so-called open palm technique, in which the defects were left for secondary healing.[21] The use of open palm technique has a higher recurrence rate (32%) and a greater limitation of the range of motion in long-term evaluation.[22]

Segmental aponeurectomy (also called segmental fasciectomy) is a procedure that removes approximately 1cm segments of affected aponeurosis without mobilizing or undermining the skin. Part of the affected tissue is left in situ.

Radical aponeurectomy (also radical fasciectomy), i.e. complete removal of the whole aponeurosis, was based on the principle that DD is an analogue to a tumor. This method, however, is associated with a high postoperative morbidity. A lower risk of recurrence with this method has not been demonstrated.[7]

Dermofasciectomy is a method in which the affected aponeurosis, including the affected skin, is removed. The resulting defects are mostly covered by full thickness skin grafts. The advantage of this procedure is reduced risk of recurrence by radical removal of the cord, including pathologically changed skin, which may contain myofibroblasts responsible for early recurrence. The main disadvantage is a longer post-operative immobilization with regards to the

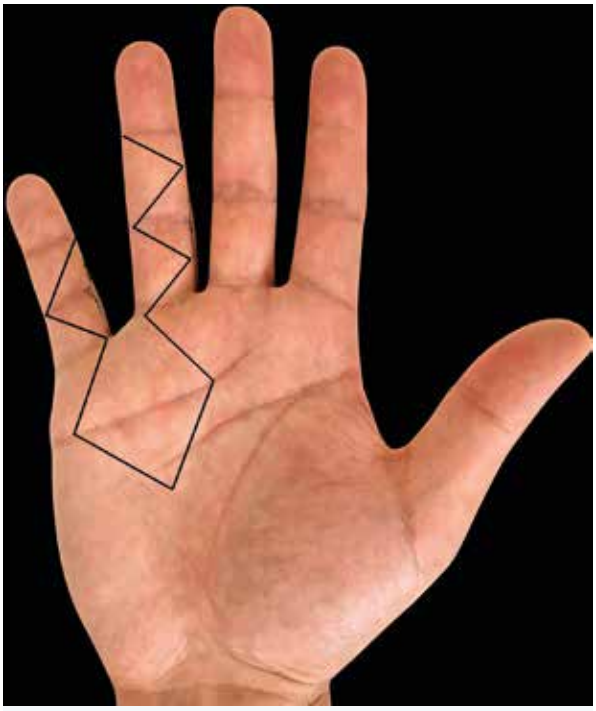

Fig. 7. Incisions according to Hurst

healing of the skin graft. This method is indicated especially in case of relapses or in young patients with an aggressive form of the disease.

If we want to evaluate the recurrence rate after various treatment options, we must be aware of one important thing – whether it is possible to satisfactorily define recurrence as itself and how. The limits of recurrence have often been defined in the literature differently and it was not possible to make comparisons in various studies. Significantly different definitions for recurrence limits made almost impossible the effectiveness of individual treatment options to compare. Until recently, there has been some unification of the criteria that the condition is defined as recurrence. The recurrence is now considered as condition where the contracture of the joint (or the extension deficit) returned to 20 to 30 degrees. It is in the case of previously treated joint to full extension or a maximum of 5 degree limitation of extension.[16] Most current studies are based on this definition. This definition often does not correspond to the patient's own disability, and may therefore be more academic than practical or functional. For one patient, a 20-degree extension deficit may be functionally significant, for another, this may be no problem and an extension deficit of 50 to 60 degrees may only be considered significant. Therefore, the limit of recurrence cannot be specified precisely in relation to the functional results of the therapy, which is generally important in hand surgery. This discrepancy between the recurrence defined in literature and the "functionally" significant recurrence together with the considerable heterogeneity of the disease make it difficult to compare data published in literature and to compare the effectiveness of the individual treatment options. On the other hand, we have no other choice than to use partially academic criteria for clinical trials in DD, but we should always consider the functional aspect and not to forget the disability noticed by the patient.

DISCUSSION

Although new mini-invasive techniques have begun to be promoted in recent years in DD treatment, classical open surgical therapy remains the gold standard of DD treatment. In most cases, limited aponeurectomy (possibly extended with removal of cords in individual fingers) appears to be the most effective technique in the case of primary disease. The disadvantage of open surgery is both longer recovery and also the risk of complications during healing or the risk of neurovascular structures damage. It can also be said that the results of surgical therapy are dependent in some extent on the surgeon's experience and skills.

Disadvantages of open surgical procedures are eliminated by mini-invasive techniques, however lower effectiveness and higher risk of recurrence must be expected. They have a good effect especially in the case of elderly patients or patients who cannot undergo surgery for any medical or social reason. Mini-invasive operations can also be useful for advanced contractures of multiple fingers. In these cases, the mini-invasive procedure can precede a few weeks the radical procedure, thereby improving operational comfort during radical surgery and accelerating post-operative rehabilitation. The use of CCH provides comparable results to open surgical therapy, but we need to wait for a definitive assessment of the effectiveness of CCH treatment. We cannot also forget the high economic burden of CCH treatment.

Previously published results of expert studies investigating the efficiency of various DD treatment regimens are still insufficient to determine, which treatment methods are "better" or "worse".[23] Given the significant heterogeneity of disease manifestations, inconsistent criteria for the recurrence, both academic and functional, dependence of the treatment effect on the personal experience and surgeon's skills (especially in fasciectomy) and other factors, it is possible to say that a randomized and blinded study to clearly answer these questions can not be done now or in the future. The situation is completely different for example to drug studies that can be randomized and double-blinded. Thus, the "heretical" question can be asked whether we will ever have enough information and experience in the future to be able to accurately assess the effectiveness of these treatments.

We also have to remember that the optimal goal of DD therapy is to remove the contracting tissue with least possible intervention on the soft tissues of the hand, and therefore, with the least risk of complications. After every open surgery, there is more or less scar tissue produced, which limits the movements of the finger, and, if further reoperation in case of recurrence is necessary, increases the risk of perioperative damage to the vessels, nerves or skin cover. Every other open surgery at the site where it was previously operated also means a worse prognosis of healing. This does not have to be the case for post-CCH surgery, when collagenase has been shown to provide safe future fasciectomy.[24] However, we should still await long-term CCH treatment results, including this aspect. Only after gaining further experience, we will be able to tell more precisely for what disease stage or for which groups of patients this treatment may have the greatest benefit.

CONCLUSION

Dupuytren's disease is clinically heterogeneous and has a significant impact on the function of the hand. We now have a range of therapeutic procedures available for DD, ranging from conservative, mini-invasive to open surgical methods. The method of treatment should be chosen not only on the basis of the clinical manifestations of the disease but also with regards to other medical, functional and social aspects of the disease. Dupuytren's disease should be treated at specialized hand surgery departments that are able to offer a whole range of treatments, from nonsurgical to mini-invasive or surgical.

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SURGICAL TREATMENT OF MELANOMA

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SUMMARY

Malignant melanoma is a serious disease, the incidence of which rises. Since the most important treatment method is sufficient wide skin and subcutaneous tissue excision, plastic surgeon is often the only specialist who is able to close the resulting defect. This paper deals with recommendations and treatment options for malignant melanoma from the point of a plastic surgeon. The primary width of excised safety rim of healthy tissue with regards to the depth of melanoma invasion differs. Safety margin is 0.5 cm for melanoma in situ, 1 cm in Breslow up to 2 mm and 2 cm in Breslow over 2 mm. Furthermore, there is indication for sentinel lymph node biopsy, which should be performed in melanoma with Breslow over 1 mm, and in risky melanoma in Breslow above 0.75 mm. Every patient with stage IIB malignant melanoma and above according to TNM classification should undergo adjuvant therapy in a specialized centre. Ideal condition for the patient is a permanent and close cooperation between a dermatologist, oncologist and plastic surgeon, who supplement each other in diagnostics, therapy and follow up of the patients.

KEYWORDS

Melanoma, surgery, plastic surgery, treatment, malignant melanoma, skin tumour, cancer

NATURE OF THE DISEASE

Malignant melanoma (MM) is a malignant disease of pigment cells of the basal layer of epidermis – melanocytes. These differentiate from embryonal neural crest and migrate from there to the whole body. They have therefore a great migration potential, which they re-adopt during malignant dedifferentiation and this is one of the reasons of frequent metastatic spread and aggressive behaviour of this tumour. Although it comprises only 3% of skin malignancies, it is responsible for 75% of deaths due to malignant skin tumours.[1,2]. Another reason for concern about this disease is its increasing incidence in the western world, and its faster increase in incidence compared to other malignancies.[1]

Mainly fair-skinned people with fair hair and light eyes are in danger of malignant melanoma. These people almost never get a sun tan and on the other hand they have a tendency to get a sunburn (phototype I and II according Fitzpatrick classification)[1]. Furthermore, the risk factor for delayed development of MM is a burn with vesicles in early childhood, exposure to UVA and UVB irradiation. Greater risk to develop MM is reported among people with greater occurrence of dysplastic nevi. There is also a slightly higher risk in 1st degree relatives of patients with melanoma. There is also a 2nd primary melanoma observed in 3–5% of patients with a history of MM in the past.[3]

Localization of MM in women and men differs; in women it is more common on the lower limbs, in man in cranial part of the trunk and it is related with the area of skin exposed to sun.[4] Women in general have a better prognosis of MM, which is probably related with better prognosis of malignant melanoma on the limbs.

DIAGNOSTICS

In order to differentiate risky lesions from less risky, it is possible to use a simple aid, so called ABCDE rules:

A – asymmetry – irregular shape of the lesion

B – borders – unclear borders, could be blurred

C – colour – presence of two or more different shadows from brown to grey, blue to pink and red

D – diameter – diameter over 6 mm, or recent change of the size of the lesion

E – evolution/evolving/enlarging – morphological changes over a short period (months)[5]

Clinical description using this scheme is only supportive and the method of first choice in the diagnostics of malignant melanoma is obviously a dermatoscopic examination in the hands of an experienced dermatologist.

TYPES OF MALIGNANT MELANOMA

Lentigo maligna

It is a light pigmented map-shaped spot, typically on the face of the elderly, mainly women. The occurrence is mostly on skin exposed to sun.[6] It can reach also a large diameter. It is a precancerosis of melanoma, melanoma without invasion, which may progress to lentigo maligna melanoma, which already shows signs of invasion. Transformation to invasive form is at 30–50%.[7,8] (Fig. 1.)

Superficially spreading melanoma (SSM)

It is the most common type of MM; it comprises 60–70% of melanomas.[5] It shows horizontal growth pattern in skin and therefore its prognosis during early surgical therapy is

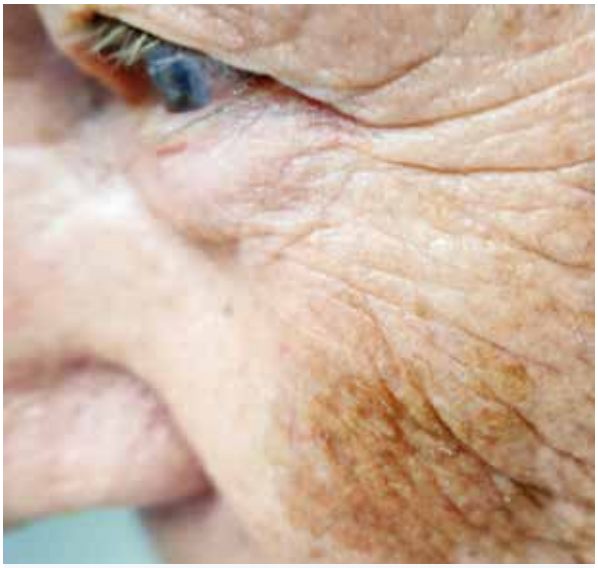

Fig. 1. Lentigo maligna

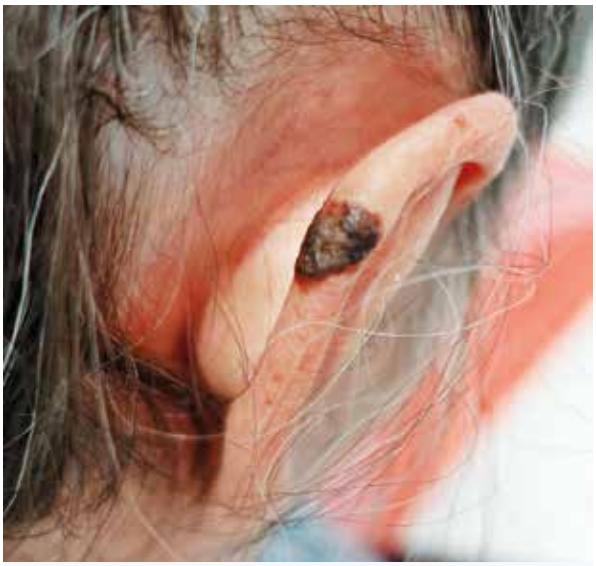

Fig. 2. Superficially spreading melanoma of the right ear

favourable.[2,5] With longer duration, there may be a change of growth from horizontal to vertical; macroscopically is usually observed development of nodularity; this is then referred to as secondary nodular superficial melanoma. This change of growth dramatically worsens prognosis of the disease. (Fig. 2.)

Nodular melanoma (NM)

Usually dark pigmented elevated lesion, which is primarily microscopically characterized by vertical growth, and which is the reason for poor prognosis of the disease.[2] (Fig. 3.)

Special types of cutaneous malignant melanoma

Amelanotic melanoma

Tumour cells of amelanotic melanoma lost the ability to synthesize melanin pigment. We find inconspicuous nodular and usually pink lesion. This inconspicuous character of the lesion is the reason for common late diagnosis, and it is not an exception that it is diagnosed already in a stage of generalization, which results also in very poor prognosis.

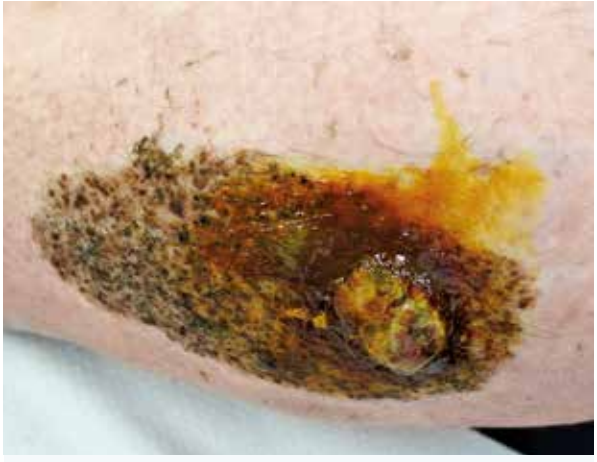

Fig. 3. Nodular melanoma developed in a congenital nevus on the calf in a 51-year-old patient, Breslow 12 mm, Clark V

Acral lentiginous melanoma

Specific and aggressive type of melanoma, which is not very common in the Central Europe. It is more common in population with darker skin colour, in whom the types of melanoma that are more common in our area are not very frequent.[3] Acral lentiginous melanoma occurs either on the palms or on the soles, or under the nail (subungual melanoma). Subungual location may be mistaken with a hematoma after nail bed contusion. Compared to this, it has no tendency to grow away, but on the contrary, it gradually leads to ulceration in the nail area. Thumb is the most frequently affected; other fingers are rare.[1] Prognosis of acral lentiginous melanoma is serious.

Mucosal melanoma, eye melanoma

Mucosal melanoma may be encountered virtually in any mucosal surface, it is most frequently observed in oral parts of the gastrointestinal tract, in the proximal part of the respiratory tract, rectum, vulva and vagina. Its poor prognosis is related with often difficult clinical examination. Mucosal melanoma affects the Asian population more frequently.[10]

Uveal melanoma is the most common malignant intraocular tumour.[11] The group of uveal melanomas includes malignant melanoma of the iris, ciliary body and choroidea; the last is the most common.[11]

This subchapter is mentioned rather for completeness; it is a disease, which is not commonly treated by plastic surgeons.

Melanoma of unknown primary origin

In a small percentage of malignant melanoma patients, there is a possibility of regression of the primary tumour, and there are only metastases present. This probably occurs during an excessive growth of the tumour with its subse-

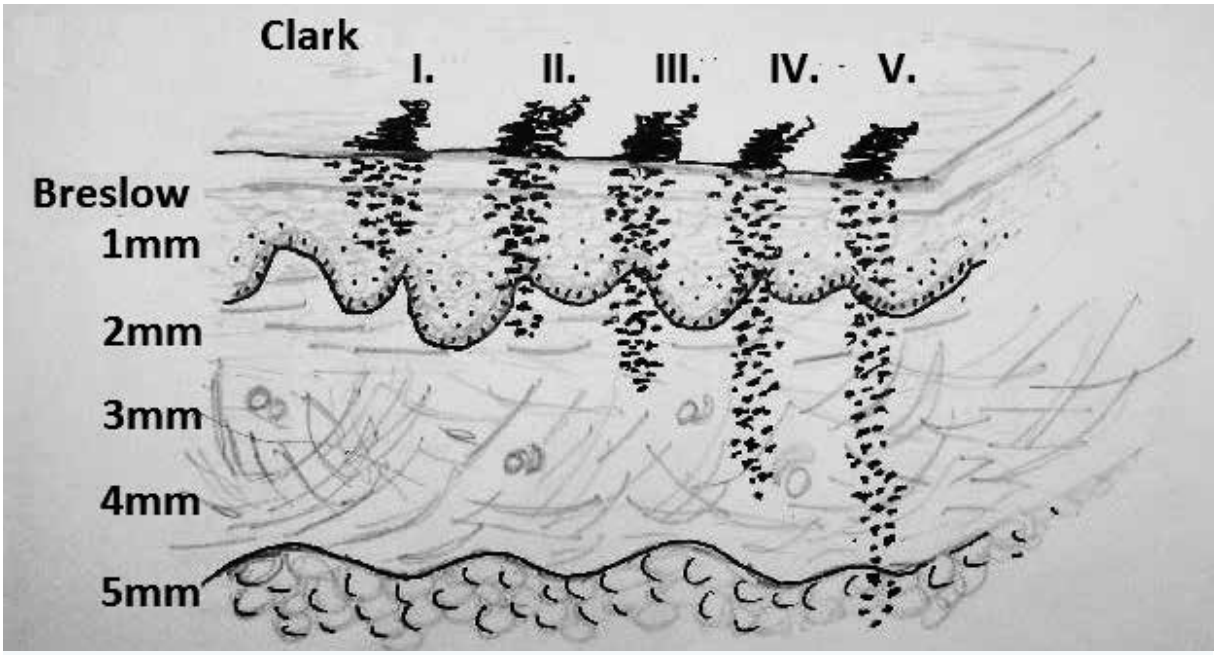

Fig. 4. Breslow, Clark classification

quent necrosis due to insufficient nutrition of a rapidly growing tumour.

CLASSIFICATION

Breslow classification

Depth of invasion in millimetres is evaluated. It is measured from the upper border of stratum granulosum of epidermis. Evaluation of invasion according to Breslow is historically the most recent classification, but it is currently considered to be the most important prognostic factor of the disease and according to its value is chosen the extent of surgical excision and possible application of adjuvant therapy.[12]

Clark classification

It is an evaluation of invasion to individual histological layers of the skin. Grades I–IV (V) are evaluated. Clark I is invasion that does not exceed the basal membrane of the epidermis, Clark II is invasion to the papillary layer of dermis, Clark III is at the border of papillary and reticular layer of dermis, Clark IV reaches to the reticular layer and sometimes is reported also Clark V, which is invasion of MM to the subcutaneous fatty tissue.[13] This classification is criticized that it is associated with a subjective evaluation of the pathologist.[12] (Fig. 4.)

METASTATIC SPREAD OF MM

MM spreads early and by hematogeneous as well as lymphatic way. Lymphatic metastases are reported as satellite metastases; these are found in a distance of 2 cm from the tumour or scar after previous excision.[5] Another type of lymphatic spread are so called in-transit metastases. These are present more than 2 cm from the tumour or scar and they occur in the direction towards the draining lymph nodes; they commonly create a strip of small pigmented lesions from the tumour to the regional lymph nodes.[14] (Fig. 5.)

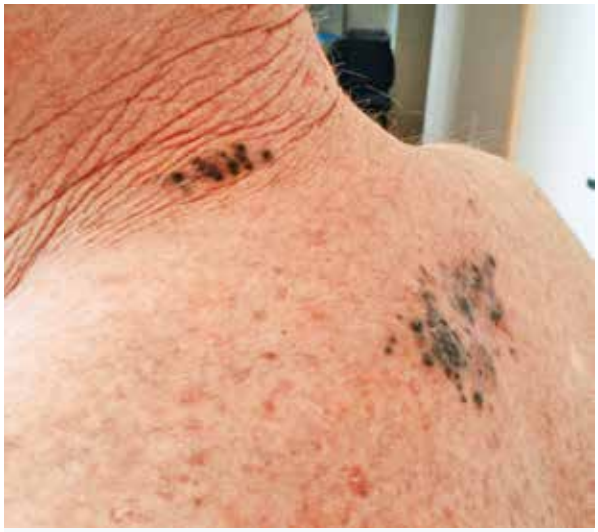

Fig. 5. Satellite metastases around the scar after excision of melanoma in the interscapular area; in-transit metastases in the area of the neck dorsally on the left side

Another option of lymphatic spread is impairment of regional lymph nodes. These are micrometastases and may be detected only by histological examination or macrometastases, visible on ultrasound, CT or on palpation during clinical examination.

Hematogeneous spread of MM is most commonly to the liver, lungs, brain, bones, GIT, but virtually there is a possibility of hematogeneous spread to any organ.[15]

PROGNOSIS

Definite prognostic factor of malignant melanoma is depth of invasion; patients with Breslow less or equal to 1 mm have a 5-year survival of 90%, in case of invasion of 4 mm is 5-year survival only 45%. This data is the basis for the extent of surgical and adjuvant therapy.[16]

THERAPY

Surgical therapy

It is the treatment of first choice in most localized diseases with a relatively high chance for complete recovery.[2,9] The condition is early diagnosis and sufficient radical surgical therapy. Extensive studies show that patients with malignant melanoma, in accordance with the depth of invasion in mm (Breslow), benefit from wide skin and subcutaneous tissue full thickness excision down to adjacent fascia. Previously performed excision of fascia is not performed anymore.[17] The size of the resulting defect is often the reason why these patients should be treated at Plastic Surgery Units.

Width of the safety rim to healthy tissue:

- Lentigo maligna (i.e. carcinoma in situ) – **0.5 cm**
- Breslow ≤ 2 mm–**1 cm**
- Breslow > 2 mm–**2 cm**[1]

In the US guidelines, it is possible to find the recommended rim of healthy tissue of 2 cm already from Breslow 1 mm. It is possible to adopt such an approach that a patient with melanoma benefits from every millimetre which we remove, while the minimum is 1 cm in case of invasion to 2 mm and 2 cm in case of a deeper invasion. Rim of healthy tissue is measured and marked on skin before infiltration with an anaesthetic solution; photodocumentation is usually performed in order to prevent doubts about sufficient radicality, because extensive retraction often occurs after placement of the specimen to a fixation solution.[18]

Sentinel Lymph Node Biopsy (SLNB)

Sentinel Lymph Node is the first lymph node that drains a particular part of the body. Its examination provides valuable information about a possible spread of melanoma, because it is the first lymph node, which drains lymph from the tumour area[19]. Sentinel lymph node may be detected with a radiopharmaceutical, usually Tc^{99} injected to the area of the tumour (performed at the Nuclear medicine unit). The signal is detected at an operation theatre with a gamma probe and a particular lymph node is removed and sent for histological examination.[20] Sentinel lymph node biopsy is indicated in all melanomas with Breslow ≥ 1 mm, in prognostically more serious melanomas already in Breslow ≥ 0.75 mm. Prognostically more serious refers to melanomas with ulceration, signs of regression, count of mitoses more than 1 to 1 mm^2. SLNB is a staging examination, which means that its result is used to determine further management. In case there are malignant cells found in the sentinel lymph node, dissection of regional lymph nodes should be performed. It should therefore be considered whether we perform sentinel lymph node biopsy in patients, who are not medically fit to undergo such extensive procedure as e.g. block neck dissection.[21] Sentinel lymph node biopsy is not performed, if there is a suspicion of metastatic lymph node impairment; this includes palpable lymphadenopathy or ultrasound signs of tumour lymphadenopathy. Dissection of regional lymph nodes should be a part of the primary surgical therapy in such a situation.[9]

According to the current guidelines, it is not an error to remove a lesion of unclear nature with a 1–3 mm rim of healthy tissue and based on the result of a histological examination proceed to re-excision of the scar with sufficient rim and to possible sentinel lymph node biopsy. Aforementioned rim of 1–3 mm does not impair lymphatic drainage, therefore there will subsequently be the correct sentinel lymph node marked with a radiopharmaceutical.[2]

0	Melanoma in situ, no lymph node impairment, no distant metastases
Ia	Tumour with Breslow up to 1 mm without ulceration, no lymph node impairment, no distant metastases
Ib	Tumour with Breslow up to 1 mm with ulceration or with Breslow 1.01–2 mm without ulceration, without lymph node impairment, without distant metastases
IIa	Tumour with Breslow 1.01–2 mm with ulceration or tumour with Breslow 2.01–4 mm without ulcerations, no lymph node impairment, no distant metastases
IIb	Tumour with Breslow 2.01–4 mm with ulcerations or tumour with Breslow above 4 mm, without ulceration, no lymph node impairment, no distant metastases
IIc	Tumour with Breslow over 4 mm with ulcerations, without lymph node impairment, without distant metastases
IIIa	Tumour of any Breslow without ulcerations, with 1–3 positive lymph nodes for micrometastasis, without distant metastases
IIIb	Tumour of any Breslow with ulceration with 1–3 positive lymph nodes for micrometastasis or tumour of any Breslow without ulceration with 1–3 positive lymph nodes for macrometastasis or in-transit/satellite metastases, no distant metastases
IIIc	Tumour of any Breslow with ulceration with 1–3 positive lymph nodes for macrometastasis or in-transit/satellite metastases, tumour of any Breslow with presence of minimally 4 metastatic lymph nodes or in-transit/satellite metastases with lymph node impairment
IV	Tumour of any invasion and any lymph node impairment with the presence of distant organ metastases

Table 1. Stages of malignant melanoma[22]

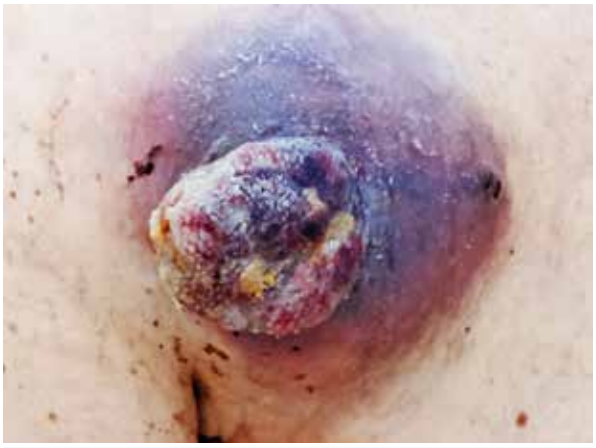

Fig. 6. Patient with a recurrence of melanoma in a scar above scapula on the left after sufficient wide excision

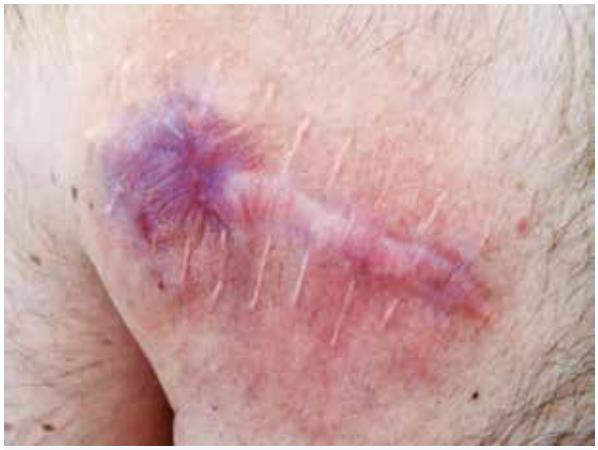

Fig. 7. Patient after six months of combined therapy with BRAF and MEK inhibitor

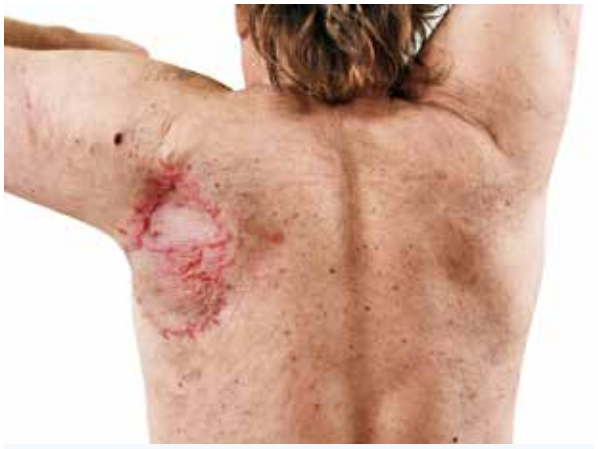

Fig. 8. Patient 4 months after radical surgical procedure

Adjuvant therapy of malignant melanoma – review of current options

Adjuvant therapy in patients with melanoma is indicated based on the stage of the disease, from stage IIB inclusive (Table 1).[2]

Immunotherapy

INF alpha. Interferon alpha is a cytokine, which improves anti-tumour immunity with a mechanism, which is not clear yet.[5] It is used for adjuvant treatment of melanoma patients and prolongs progression free survival. There are 3 various dosing schedules used worldwide. Their results are comparable. INF alpha is usually administered for 12–24 months as a subcutaneous injection 3 times a week, which is managed by the patients alone at home usually quite well.[5] Early adverse effect of INF alpha therapy includes so called "flu-like" syndrome, which is comprised of fever, fatigue, and joint pain. It has been treated with symptomatic therapy.

Ipilimumab. It is a monoclonal antibody targeting CTLA 4 receptor of cytotoxic T lymphocytes. Binding to CTLA 4 receptor results in stimulation of cytotoxic T lymphocytes and thereby in stimulation of antitumor immunity.[23] This antibody acts also against other malignancies.

Pembrolizumab, Nivolumab. This is a human IgG4 anti-PD-1 monoclonal antibody (PD = programmed death). Similarly to antibodies against CTLA 4, also these activate immunocompetent cells and thereby non-specifically reduce escape of tumour cells from the action of the immune system.[24]

Since immunostimulating antibodies against PD 1 and CTLA 4 act to different receptors, it has been demonstrated in clinical studies that their combination, particularly Ipilimumab and Nivolumab, results in prolongation of progression free survival and overall survival in patients with non-resectable MM.[25]

Targeted therapy

Targeted therapy means that there is a therapeutic intervention performed directly to the replication cascade using a specific inhibitor; this results in stopping of the division of tumour cells.

BRAF inhibitors – Dabrafenib, Vemurafenib

Skin melanomas in more than a half of the cases are associated with mutation in the BRAF gene, particularly BRAF V600E, based on which occurs activation of replication cascade with subsequent uncontrolled division of melanoma cells. Inhibitor of BRAF protein blocks this cascade with subsequent regression of the disease.[26]

MEK inhibitors – Trametinib, Cobimetinib

They influence the next step of the replication cascade, i.e. immediately after BRAF inhibitors, with a similar mechanism.

Recent studies show that patients with BRAF mutation benefit from combined therapy using MEK and BRAF inhibitor. There is prolongation of progression free survival and overall survival with regression of adverse effects of targeted melanoma therapy (specific skin toxicity - hyperkeratosis of soles and palms, development of skin papillomas and spinocellular carcinomas).[26] Unfortunately, resistance on

targeted antibodies in monotherapy and in combination occurs within months and years, which results in a relapse of the disease. (Fig. 6, 7, 8.)

Chemotherapy

This chapter is included for completeness. With regards to the current use of modern and much more efficient treatment options during the recent decades, usage of chemotherapy in non-resectable malignant melanomas is subsiding. Some units still use Dacarbazine in monotherapy in specific cases.

Specific treatment options in MM

Hyperthermic limb perfusion

This method had been repeatedly used in the past and was abandoned already from the 50' of the 20th century and it is currently experiencing a comeback. It requires a specific patient – disease localized only to a single limb, particularly distal part of thigh and more distally, or distal arm and more distally. This method is complicated and demanding for the patient. The affected limb is perfused with a concentrated cytostatic solution heated usually to 40–41°C after cannulation of the arterial and venous system and it uses Melphalan, Dacarbazine, Cisplatine and TNFα.[27,28]

Radiotherapy

It is reserved for specific situations in patients with MM and it is usually based on an agreement of a multidisciplinary team. This may be considered e.g. as an adjuvant radiotherapy after excision of satellite or in-transit metastases, excision of extensive mucosal melanomas, dissection of significantly impaired lymph nodes, which is however commonly associated with lymphedema. Furthermore, it is used as a palliative therapy of metastases to the brain or extensive non-resectable in-transit or lymph node metastases.[29]

Intralesional application of cytostatics

MM spreads specifically to the skin, and therefore these lesions are easily accessible to local treatment in terms of cauterization or intralesional application of cytostatics. This is of course palliative therapy rather than curative.[2]

CONCLUSION

Malignant melanoma is, despite great therapeutic advances in recent two decades, especially in biological therapy, still a malignant disease with a very serious prognosis and it has a rising incidence, where the hope for complete recovery is only in patients with early detection of the disease. Therefore, every suspicious skin lesion should be excised and histologically examined. When confirming the diagnosis of melanoma, there should be re-excision of scar with sufficient rim of healthy tissue performed and according to the depth of invasion should also be possibly performed sentinel lymph node biopsy. Every patient with the diagnosis of melanoma should be followed in a unit by an experienced team and available modern adjuvant therapy.

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Figures 1, 2, 3, 8 source: Department of Plastic Surgery, Královské Vinohrady University Hospital
Figures 4, 5, 6, 7 source: author

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INDEX

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POSTOPERATIVE FIXATION AFTER REPOSITIONING OF PREMAXILLA IN A PATIENT WITH BILATERAL CLEFT LIP AND PALATE – CASE REPORT

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SUMMARY

This article presents orthodontic-surgical treatment in an eight-year-old patient with bilateral cleft lip and palate where premaxilla was surgically repositioned in the mixed dentition stage. By cranial and dorsal insertion of the premaxilla were created satisfactory occlusal relationship for ongoing eruption of permanent teeth, together with functional lip closure, improved pronunciation and a positive change in appearance of the centrofacial area. Reposition of premaxilla was associated with bilateral alveolar bone grafting of the cleft defect with cancellous bone from the iliac crest. Based on the model surgery were prepared rigid orthodontic wires, which ensured postoperative fixation of the segments of the upper jaw. The patient was wearing band fixed appliance for another 6 months after surgery. Healing was uncomplicated, the new position of the premaxilla was stable and more physiological. This procedure was friendly for a child patient and did not require fixation of the jaw segments by Sauer splint.

KEYWORDS

Bilateral cleft lip and palate, reposition of premaxilla, fixed appliance, orthodontic--surgical cooperation

SUMMARY

Bilateral cleft lip and palate is often associated with unfavourable position of the premaxilla, which deteriorates further with growth of the patient. Correction of this type of cleft belongs among the most difficult. It requires basic surgical reconstructions that concern adjustment of the shape and relations of dental arches and arrangement of teeth. Premaxilla in a patient with bilateral cleft lip and palate is shifted to the front and caudally, it is fixed only to the vomer in unstable position with various extent of movements[1]. Location of premaxilla is attributed also to the functional and morphological insufficiency of orbicularis oris muscle[2]. The patient has, apart from a serious aesthetic handicap of the centrofacial area, also difficulties during the mouth closure, chewing and speech, which results in various psychosocial problems.

REPOSITIONING OF PREMAXILLA

Correction of the position of premaxilla is based on its shift cranially and backwards, in adjustment of the slope of the alveolar process, and possibly in rotation of the whole segment. The procedure is, according to the anatomical situation, either surgical or orthodontic-surgical. Correction of the position of premaxilla is possible in various developmental phases of the stomatognathic system.

In some patients with total bilateral cleft a severe deviation of premaxilla is obvious right after the birth (Fig. 1A) and primary surgical reconstruction of the lip and nose is very demanding. Therefore in the past there were also resections of the whole protruding intermaxillary segment[3] or early surgical impaction of premaxilla[4] performed.

In 1983, Vargervik demonstrated an unfavourable effect of early surgical procedures in the area of the premaxilla on further growth of the upper jaw[5]. Mainly due to his research, the age limit for surgical repositioning of the frontal segment of the maxilla was moved to higher age categories (6 years and more) and it was started to be combined with reconstruction of the alveolar process with cancellous bone at the site of the cleft defect. This operation was indicated in the phase of mixed dentition[6].

Possible presurgical orthodontic (orthopaedic) repositioning of premaxilla within a moulding procedure in newborns can be problematic in bilateral cleft lip and palate patients. Such intervention is advantageous and effective in indicated

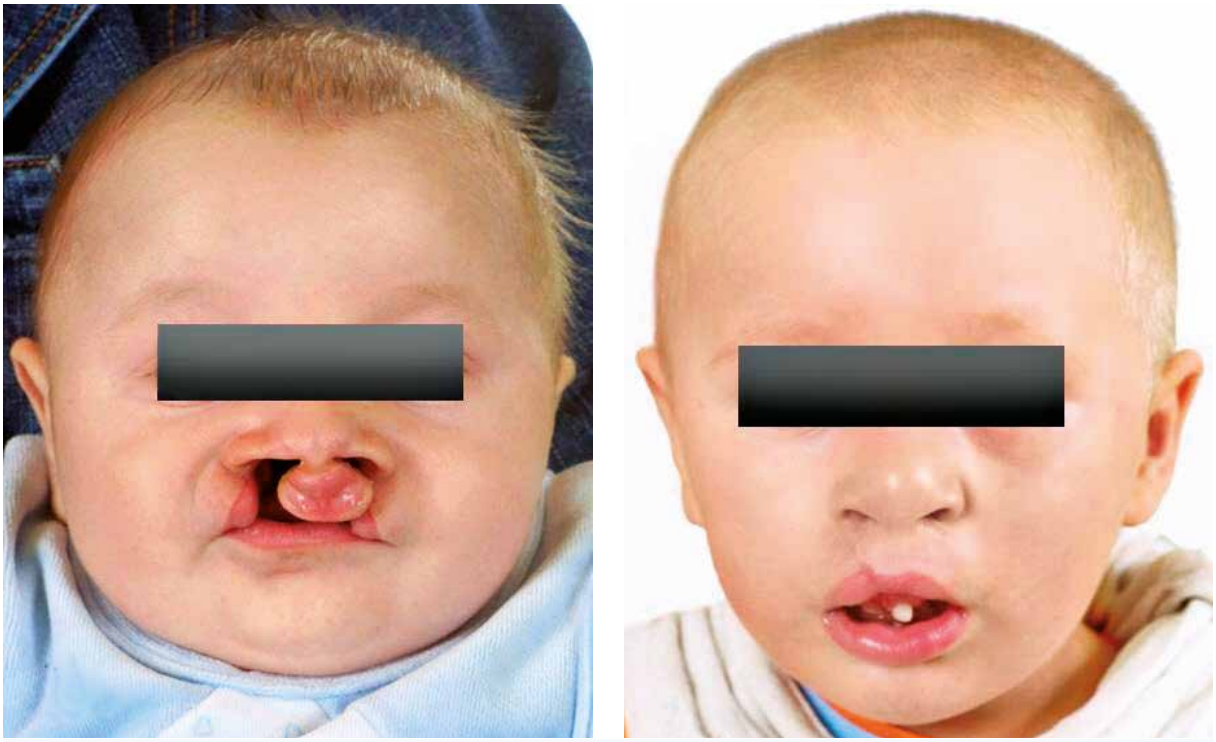


Fig. 1 A, B. The face of the patient before primary surgical correction of the lip at the age of five months and before palate reconstruction in 22 months

cases, when it is necessary to reduce the distance of each segment of the cleft maxilla and thereby significantly reduce the tension in the area of soft tissues in primary lip reconstruction. However, the effect of moulding on the shape and further growth of maxilla was not demonstrated[7, 8, 9].

As a suitable option of therapy seems the combination of surgical repositioning of premaxilla and simultaneous reconstruction of the cleft defect in alveolar process with cancellous bone between the eighth and eleventh year of age. Supplementation of bone ensures stability of the new position of repositioned premaxilla[2, 10]. Essential for successful healing of premaxilla in the desired position is its rigid stabilisation. Fixation of repositioned frontal segment of maxilla may be performed by a surgeon with skeletal fixation using microscrews and a surgical plate to the vomer or to the lateral maxillary segments[11]. The risk of this procedure is a negative impact to the growth centre of maxilla and possibility to impair teeth germs. Another option to ensure stable healing of premaxilla is usage of a Sauer splint, rigid resin bite plates and/or fixed orthodontic appliance. Until complete healing of repositioned premaxilla, it is also recommended to exclude all occlusal interferences, e.g. with bites on molar occlusion surfaces, or individual resin removable plate on the lower dental arch[12, 13]. Reference literature provides case reports of successful orthopaedic repositioning of premaxilla without the use of surgical procedures only with the help of an orthodontic pull[14]. Surgical repositioning of premaxilla in adult patients with a cleft may be a part of an orthognathic operation.

The following case report demonstrates repositioning of premaxilla in an eight-year-old boy as one of the phases of a complex interdisciplinary treatment of the patient with bilateral cleft lip and palate.

CASE REPORT

A boy with a total bilateral cleft of the maxilla was born as a twin from a 1st risky pregnancy, the second child – sister – is healthy; family history is negative with regards to the patient's impairment. Labour with Caesarean section was accomplished without complications, as well as the postpartum adaptation.

The first examination of the boy at Orthodontic department of the Centre for treatment of congenital head and neck disorders, Centre for treatment of facial clefts, University Hospital Královské Vinohrady in Prague took place within the preoperative examination on admission for planned primary reconstruction of the lip at the age of 5 months (see Figure 1A). At this examination, there was already obvious significant protrusion of premaxilla frontally and caudally and transversal collapse of lateral maxillary segments. At the age of 22 months was performed reconstruction of the palate (Fig. 1B). The boy suffered from persisting significant transverse narrowing of the maxilla, insufficient lip closure, sucking in of the lower lip at the age of three years. We therefore attempted to improve the anatomical relations with the application of a palate plate with a transversal expansion screw (Fig. 2 A, B, C) on which the patient got surprisingly well adapted. After four months of appliance usage, the boy learned how to open mouth better; the lip closure improved and the mother reported also improved speech. Transversal expansion of lateral segments demonstrated significant

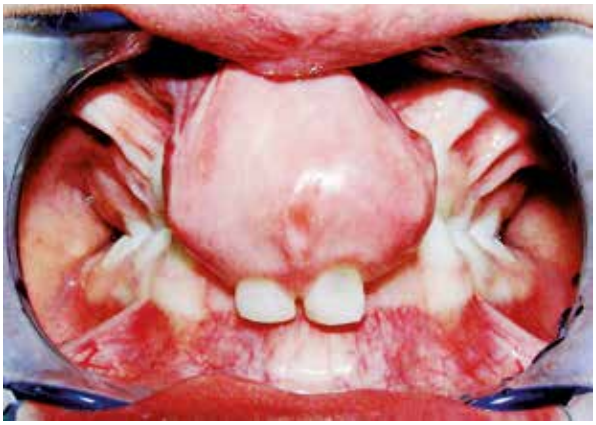


Fig. 2 A, B, C. Temporary teeth of the patient at the age of three years (A), palate plate with a screw for transversal expansion of lateral jaw segments and elastic segment that blocks the movement of premaxilla caudally (B). Appliance in the mouth of the patient (C)

tendency to recurrence, long-term usage of expansion appliance was therefore needed. Exchange of teeth started at the age of seven years with the eruption of permanent molars, eruption of incisives was delayed.

Within interdisciplinary treatment plan was indicated repositioning of premaxilla after eruption of upper permanent incisors. This occurred at the age of eight years of the patient, when a band fixed appliance was applied on the upper dental arch (Fig. 3 A, B). The upper dental model was rebuilt and thick postsurgical wires were prepared in accordance with the required position of premaxilla and an operation plate. Bands as a part of fixed appliance were placed on the permanent central incisors, temporary canines and first permanent molars.

During the operation was performed osteotomy of the neck of the premaxilla and its shortening by 6 mm as planned, insertion of premaxilla to the optimal horizontal and vertical position. Simultaneously was performed bilateral closure of vestibulo-oronasal communication together with bilateral reconstruction of the alveolar process with cancellous grafts from the crest of the ilium bone in a total volume of 6 cc. There were also dysplastic afunctional upper lateral incisors removed from premaxilla. External fixa-

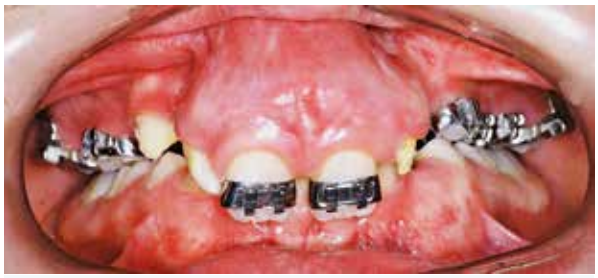


Fig. 3 A, B. Face and teeth of the patient with fixed appliance before surgical repositioning of premaxilla

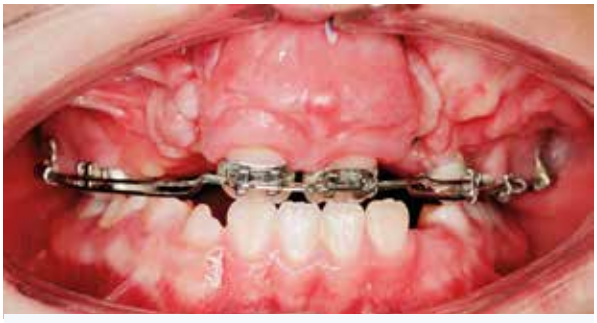
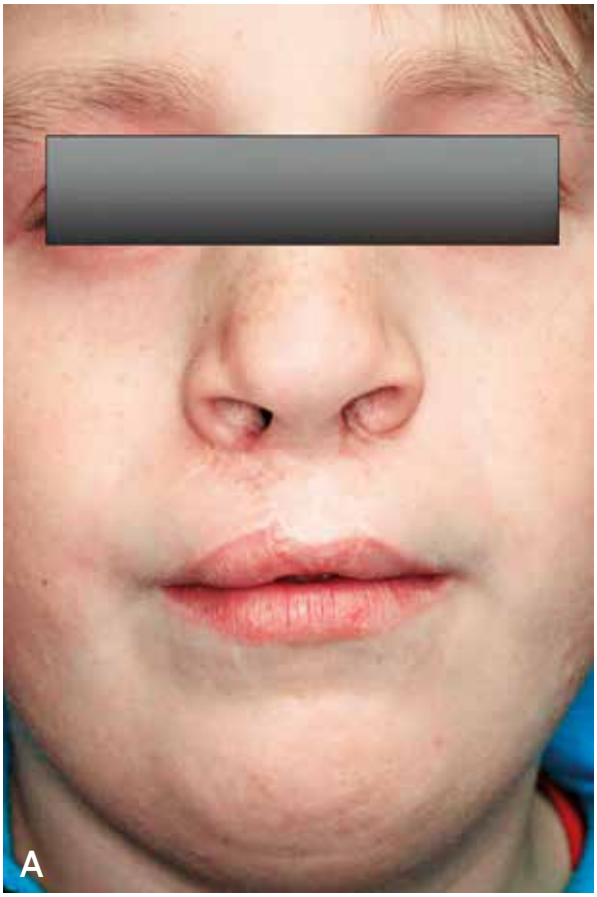
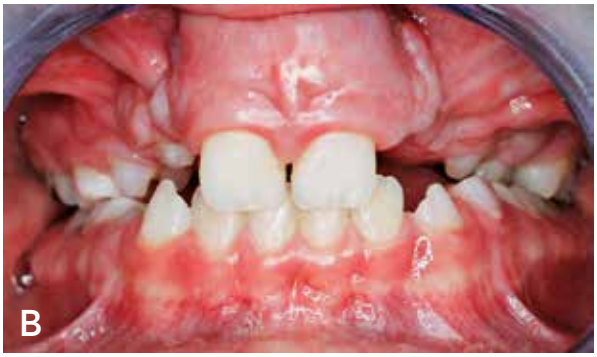


Fig. 4. Teeth of the patient with fixed appliance and thick postsurgical immobility wire three weeks after surgical repositioning of premaxilla





tion of maxillary segments was performed with fixed band orthodontic appliance with two intraoral arches (Fig. 4). The whole operated area was subsequently covered with semielastic surgical splint with plastic dressing. Postoperative course and subsequent healing was accomplished without any complications. The option to keep the fixed appliance for the whole mixed dentition period was not accepted by the patient and the appliance was removed after an agreement with the parents after six months and the patient still uses removable appliance (Fig. 5 A, B). Currently continues very slow second phase of teeth exchange; occlusion plane of the maxilla is satisfactory; bite significantly raised and the next phase of therapy with a fixed appliance again is planned after the eruption of upper permanent canines.

Comparison of the result of cephalometric analyses of lateral skull views six months after the operation demonstrated increased SNA angle (Point Sella-Point Nasion-Point A) due to the movement of point A due to cranial shift of a large premaxilla and increased ANB (Point A-Point Nasion-Point B) angle, which we attributed at the age of eight years mainly to the adaptation of the mandible to the new occlusion relations (Fig. 6 A, B; Table 1). The slope of upper central incisors with regards to the skull base and interincisival angle corrected.

DISCUSSION

In the aforementioned patient, it was already obvious in the first years of life that it will be necessary to adjust the position of the deviated premaxilla. Its caudal and ventral position caused that the patient was not able to close the mouth and while smiling and talking, there was gingiva and mucosa of the alveolar process of the frontal segment of maxilla visible. Orthopaedic impaction of premaxilla using orthodontic appliances in the early phases of development was not successful, therefore surgical revision was indicated.

It is obvious from the available literature that it is optimal to associate surgical repositioning of premaxilla with reconstruction of cleft defects of alveolar process of maxilla between the eighth and eleventh year of life of the patient[2]. Timing of repositioning of maxilla was, with regards to the choice of postoperative fixation, in our case dependent also on the condition of dentition in the upper arch.

Healing of bone graft depends on the condition of bony walls of the cleft defect and patency of fistula closure. Bone connection of maxillary segments provides fixation of premaxilla in an optimal position. If there was no surgical repositioning of premaxilla achieved during reconstruction of alveolar process with bone grafts, the result would be fixation of unfavourable position of frontal segment of maxilla.

The condition of good healing is rigid fixation of premaxilla in a new position. In the Centre for treatment of congenital head and neck disorders at the University Hospital Královské Vinohrady in Prague, Czech Republic was previously, during these operations, standardly used immobilisation of maxillary segments with Sauer splints and screws. Fixation of wires in the area of the teeth necks however results in irritation and swelling of gingiva (Fig. 7).

Fig. 5 A, B. Face of the patient and teeth six months after surgical repositioning of premaxilla

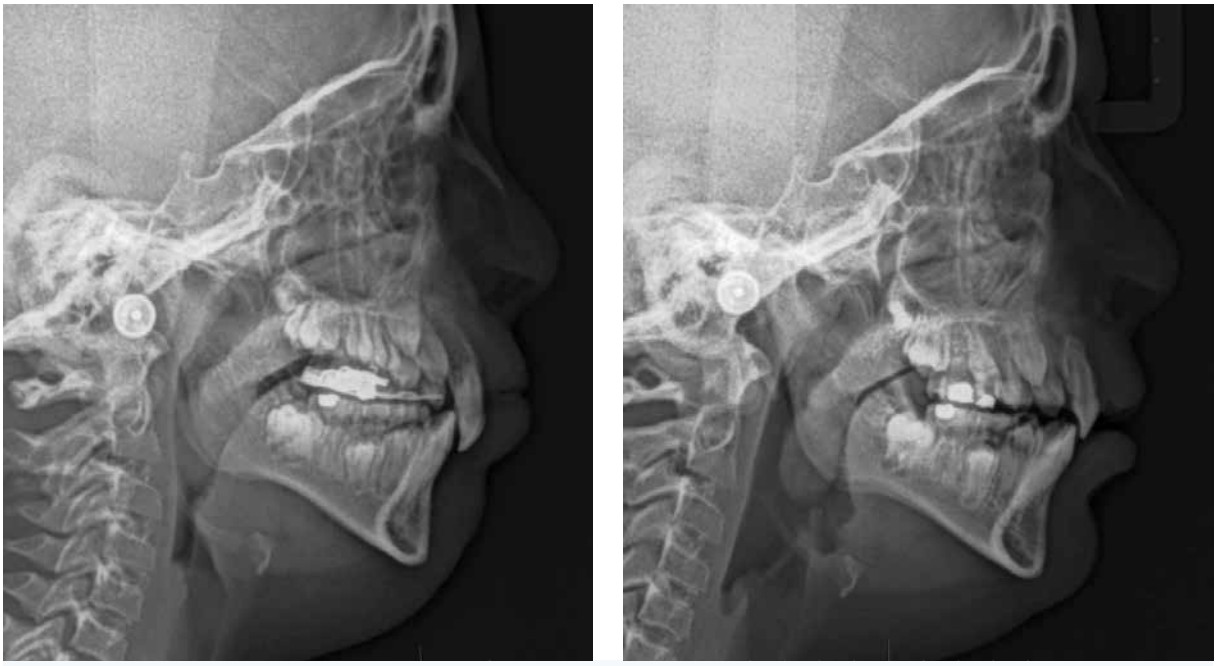


Fig. 6 A, B. Lateral cephalometric radiograph before (A) and six months after (B) the surgical repositioning of premaxilla in the day of fixed appliance removal

Values on cephalometric radiograph	Before (A)	After (B)
SNA (°)	***76.1°***	***81.7°***
SNB (°)	72.6°	74.2°
SNPg (°)	72.8°	74.2°
ANB (°)	***3.5°***	***7.5°***
Wits (mm)	***-8 mm***	***0.4 mm***
NS/ML (°)	40.5°	38.4°
1+NS (°)	***71.5°***	***85.2°***
1+NPg (mm)	7 mm	6.8 mm
1+1- (°)	***158°***	***144°***
1-ML (°)	91°	92.1°
1-APg (mm)	2.1 mm	0.5 mm
SGo/NMe (%)	62.7 %	63.8%
NS-PP (°)	***19.5°***	***12.7°***
ML-PP (°)	***21°***	***25.7°***

Table 1. Values of parameters on lateral cephalometric radiograph before surgical repositioning of premaxilla and 6 months after. ***Italics*** and ***bold font*** is used to mark the parameters, which changed the most; red is used to mark the parameters, which are out of the normal range by more than one standard deviation

(SNA = Angle: Point Sella-Point Nasion-Point A, SNB = Angle: Point Sella-Point Nasion-Point B, SNPg = Angle: Point Sella-Point Nasion-Point Pogonion, ANB = Angle: Point A-Point Nasion-Point B, Wits= Wits appraisal of jaw disharmony, NS/ML = Angle: Point Nasion-Point Sella Line/Mandibular Line, 1+ NS = Angle: Axis of the Tooth 1+/ Point Nasion-Point Sella Line, 1+ NPg = Distance of the tooth 1+ (Point Incisale Superius) and Line Point Nasion-Point Pogonion, 1+/1- = Angle: the Axis of the Tooth 1+/the Axis of the Tooth 1-, 1-ML = Angle: the Axis of the Tooth 1-/Mandibular Line, 1-APg = Distance of the tooth 1- (Point Incisale Inferius)/Line Point A- Point Pogonion, SGo/NMe = Value Ratio: Distance of Point Sella-Point Gonion/Point Nasion-Point Menton, NS-PP = Angle: Mandibular Line/Palatal Plane)

Problematic is also adequate oral hygiene of the whole splint in the postoperative period. Inflammation could subsequently impair the conditions for satisfactory healing. Therefore, it is not possible to keep this type of fixation in the mouth of the patient for a long time and within interdisciplinary consultations was searched for a solution to fix premaxilla for the whole period of healing. This may be ensured in patients with adequate teeth with a fixed appliance and

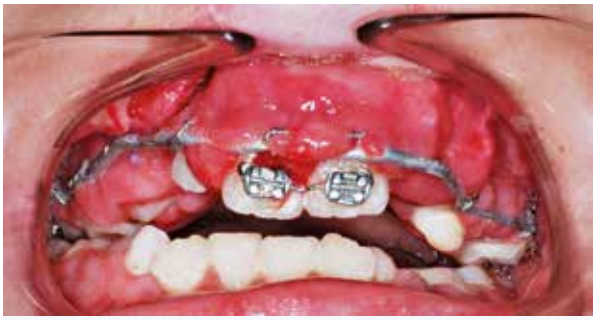


Fig. 7. Patient with a bilateral cleft lip and palate after surgical repositioning of premaxilla in which position of premaxilla was fixed with Sauer splint

supplementary rigid vestibular wire (see Fig. 4), which is fixed to supplementary slots of orthodontic bands on first permanent molars and frontally to the block of central upper incisors. The advantage of a fixed appliance is its additional possibility of orthodontic use to restore the shape of the upper teeth arch and to manage overbite of upper incisives.

CONCLUSION

Repositioning of premaxilla at the time of teeth exchange significantly improves anatomical relationships of the dental arches and thereby enables better results of orthodontic therapy; it also contributes to create a more favourable relationship of the lips and to improve lip closure. Important is also a significant change of the aesthetics of centrofacial area, which significantly affects the socialisation of an adolescent patient. In the aforementioned case was only a fixed appliance used for postoperative fixation; osteosynthesis of repositioned premaxilla was not needed. The prerequisite to use this method is the condition of teeth that enables placement of a fixed appliance. Usage of dental fixation in permanent as well as solid temporary teeth is not causing any interference to bone healing; it does not influence the germs of developing permanent teeth. Furthermore, the aforementioned method of fixation for the patient is much more convenient and gentle than Sauer splint.

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ČESKÉ SOUHRNY

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SPOKOJENOST PACIENTEK PO REKONSTRUKCI PRSU: IMPLANTÁTY VERSUS AUTOLOGNÍ TKÁNĚ

Fracon S., Renzi N., Manara M., Ramella V., Papa G., Arnež Z.M.

Úvod: Rekonstrukce prsu se stále častěji zapojuje do léčby karcinomu prsu. Je možné ji provést pomocí implantátů, nebo autologními tkáněmi. Tato průřezová studie hodnotí spokojenost pacientek a kvalitu života u žen po úspěšné rekonstrukci prsu autologní tkání nebo implantátem.

Materiál a metody: Do studie bylo zařazeno 109 žen, které úspěšně podstoupily rekonstrukci prsu mezi rokem 2007 a 2016. Pacientky vyplnily při kontrolních návštěvách dotazník BREAST-Q. Retrospektivně byly z nemocničních záznamů shromážděny další údaje týkající se komplikací, kouření, chemoterapie, radioterapie, unilaterální nebo bilaterální rekonstrukce, BMI a komorbidit. Pro hodnocení rozdílů mezi skupinou s autologní rekonstrukcí prsu (n = 50) a skupinou s rekonstrukcí prsu pomocí implantátu (n = 59) byl použit Mann-Whitney U test.

Výsledky: Ženy s úspěšnou autologní rekonstrukcí byly signifikantně více spokojené se svým rekonstruovaným prsem než ženy s úspěšnou aloplastickou rekonstrukcí prsu, měřeno pomocí prsního modulu BREAST-Q (p = 0,00596), modulu psychosociální pohody (p=0,04) a modulu sexuální pohody (p=0,00068). Dále existuje vyšší stupeň spokojenosti u pacientek, které nepodstoupily radioterapii, které neměly komplikace a měly normální BMI u skupiny s rekonstrukcí implantátem a také u nekuřaček a u bilaterální rekonstrukce pro skupinu s rekonstrukcí lalokem.

Diskuze: Zjištění naší studie jsou v souladu s údaji z literatury, které přidělují vyšší spokojenost s fyzickou, mentální a sociální pohodou a také s elementy, které mají dopad na sexuální pohodu, autologní rekonstrukci prsu.

Závěry: Autologní rekonstrukce prsu vede k vyšší spokojenosti pacientek než rekonstrukce prsu implantátem. Tato studie může pomoci pacientkám a lékařským týmům při jejich rozhodovacím procesu ohledně rekonstrukce prsu. Tato pilotní studie otevírá několik otázek, které vyžadují další zhodnocení ve větší prospektivní studii.

OLEOGEL-S10 K URYCHLENÍ HOJENÍ DONORSKÉHO MÍSTA: MONOCENTRICKÉ VÝSLEDKY KLINICKÉ STUDIE FÁZE III

Lipový B., Fiamoli M., Mager R., Jelínková Z., Jarkovský J., Chaloupková Z., Holoubek J., Suchánek I., Brychta P.

Cíl: Cílem této studie bylo zhodnocení účinnosti nového topicky aplikovaného gelu pro zrychlení reepitelizace donorských míst.

Materiál a metody: Oleogel-S10 je mast obsahující suchý extrakt z březové kůry obsahující triterpen bohatý na betulin, který byl testován v otevřené, zaslepené, prospektivní, kontrolované, randomizované, multicentrické studii hodnotící zlepšení hojení rány v donorských místech. Primární koncový parametr byl čas do uzavření rány a sekundární koncový parametr byla měření související s jizvou v době uzávěru rány a 3 a 12 měsíců po uzavření rány (POSAS, laserová kontrastní analýza LASCA, viskoelastická analýza).

Výsledky: Uvádíme výsledky z jednoho centra (Klinika popálenin a rekonstrukční chirurgie, Fakultní nemocnice Brno), kde byla provedena tato klinická studie fáze III. Celkem bylo zařazeno 32 pacientů (25 mužů a 7 žen) s průměrným věkem 41,8 let (SD, ±11,66). Průměrný rozsah donorských míst pacienta ve studii byl 56,77 cm^2 (SD, ±20,39). Střední čas hojení u skupiny s lékem (Oleogel-S10) byl 7 dnů (95% interval spolehlivosti 7–8 dnů) a u kontrol 8 dnů (95% IS 7–10 dnů). Srovnání údajů POSAS ze skupiny s lékem ukázal signifikantně menší hodnoty ve všech třech časových bodech ve srovnání s kontrolami. Perfuze jizev ve skupině s lékem dosáhla v průměru 115 perfuzních jednotek na konci léčby. Průměr byl 69,8 perfuzních jednotek po 3 měsících a 50,2 perfuzních jednotek po 12 měsících. Kontrolní místa vykazovala signifikantně vyšší hodnoty ve všech časových bodech (122,2 perfuzních jednotek, 73,9 perfuzních jednotek, 52,2 perfuzních jednotek). Signifikantní rozdíly byly detekovány ve viskoelastických vlastnostech kůže s tím, že místa léčená Oleogelem-S10 vykazovala příznivější hodnoty.

Závěr: V našich výsledcích prokazujeme významnou účinnost Oleogelu-S10 na hojení donorských míst.

NASOLABIÁLNÍ LALOK: NEJUNIVERZÁLNĚJŠÍ METODA PRO REKONSTRUKCI V OBLIČEJI

Bayer J., Schwarzmannová K., Dušková M., Novotná K., Kníže J., Sukop A.

Nasolabiální lalok byl popsán před 170 lety a nadále zůstává jednou z nejčastěji používaných metod pro rekonstrukci v obličeji. Tato technicky snadná a maximálně efektivní operace se stala skutečným základem a integrálním nástrojem každého plastického chirurga. V průběhu času bylo popsáno mnoho modifikací této techniky. V tomto článku představují autoři přehled možností provedení nasolabiálního laloku a diskutují výhody a nevýhody těchto technik.

SOUČASNÉ MOŽNOSTI LÉČBY DUPUYTRENOVY KONTRAKTURY

Kníže J., Miletín J., Nejedlý A., Chorvát M., Novotná K., Tichá P., Fibír A., Sukop A., Knížetová A.

Dupuytrenova kontraktura (fibromatóza palmární fascie, benigní neoplastická fibromatóza, Dupuytrenova nemoc), nemoc charakteristická zbytňováním a postupným kontrahováním jednotlivých částí palmární aponeurózy, je onemocnění známé a léčené po několik století. V pokročilých fázích vede onemocnění k výraznému omezení funkce ruky, což má za následek sníženou kvalitu života pacienta.

Dupuytrenova nemoc je celoživotním onemocněním s variabilním průběhem a heterogenním klinickým nálezem. Terapie je zaměřena nejen na klinické projevy nemoci, ale i ke zmenšení funkčního omezení ruky, které nemoc způsobuje. K dispozici jsou vedle konzervativních a chirurgických postupů nově i některé miniinvazivní metody. Léčba by měla být vyhrazena centrům a zkušeným specialistům, kteří se zabývají chirurgií ruky.

CHIRURGICKÁ LÉČBA MELANOMU

Novotná K., Arenbergerová M., Miletín J., Kníže J., Šandera V., Schwarzmannová K., Bayer J., Sukop A.

Maligní melanom je závažné onemocnění, jehož incidence vzrůstá. Jedná se o rakovinu pigmentových buněk kůže. V léčbě maligního melanomu je třeba postupovat v závislosti na pokročilosti onemocnění, a to jak co do rozsahu chirurgické léčby, tak co do volby léčby systémové. Indikace pro pacienta nejvhodnější léčby probíhá v rámci dermatoonkotýmu, jehož členy jsou kromě dermatologa a plastického chirurga také onkolog a patolog. Díky tomu se každému pacientovi dostane „péče na míru“. Nyní předkládáme text, který si dává za cíl přehledně a jednoduše informovat o doporučeních a možnostech léčby maligního melanomu zejména z pohledu plastického chirurga.

POOPERAČNÍ FIXACE PO REPOZICI PREMAXILY U PACIENTA S OBOUSTRANNÝM ROZŠTĚPEM RTU A PATRA - KAZUISTIKA

Koťová M., Dušková M., Leamerová E., Urbanová W., Schwarzmannová K., Novotná K., Sukop A.

Předkládaná práce představuje ortodonticko-chirurgickou léčbu osmiletého pacienta s oboustranným rozštěpem rtu, čelisti a patra, u něhož byla provedena chirurgická repozice premaxily v období smíšené dentice. Kraniálním a dorzálním posunem premaxily se vytvořily uspokojivé okluzní poměry pro prořezávající stálé zuby, vytvořil se funkční retní uzávěr a zlepšila se výslovnost i estetika centrofaciální oblasti. Repozice premaxily byla spojena s doplněním spongiózní kosti z hřebene kosti kyčelní do obou rozštěpových defektů alveolárního výběžku horní čelisti. Na základě modelové operace byl připraven rigidní intraorální oblouk, který sloužil k pooperační fixaci reponovaného segmentu horní čelisti. Šest měsíců před operací byl pacientovi nasazen horní kroužkový fixní aparát. Hojení proběhlo bez komplikací, poloha premaxily byla stabilní. Popsaný postup je pro dětského pacienta velmi šetrný, neboť pooperační fixace nemusela být zajištěna Sauerovou dlahou.

INSTRUCTIONS TO THE AUTHORS

ACTA CHIRURGIAE PLASTICAE, 2017, 59, 3–4, pp. 165-168

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