Aus der Orthopädischen Universitätsklinik Basel

Arbeit unter der Leitung von Dr. med. Andreas Müller

The use of structural and non structural bone grafts and substitutes in osteotomies and arthrodesis of the hindfoot and ankle

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Table of content

1. Abstract

Introduction: Hindfoot fusions and osteotomies implicate the decision whether to use an autologous bone graft or an osteoconductive or –inductive substitute material in order to promote bony union and/or to support the correction of an additional hindfoot deformity. Evidence directing this decision is missing. The goal of this thesis is to retrospectively quantify the use of structural and non structural bone grafts in the foot and ankle clinic of the University of Basel over a one year period and to assess the time to union achieved with each different type of graft in specific hindfoot fusions or osteotomies carried out at level of the ankle, subtalar, chopart und Lisfranc joint.

Methods: We retrospectively identified all patients who underwent fusions or osteotomies of the hindfoot from January 2006 until December 2006 using the in house electronic database „opdz“ recording all surgical procedures carried out at the institution of the University of Basel. Patients were then allocated to four treatment groups including: 1) ankle fusion and osteotomies 2) hindfoot (talonavicular, subtalar and triple) arthrodesis 3) calcaneal osteotomy and 4) midfoot arthrodesis and osteotomies. Within these major treatment categories, patients who received the same or no bone graft were further pooled in subgroups. Average time to union, rates of non - and delayed was calculated for each of the above mentioned subgroups and compared to each other within the respective treatment categories.

Results: We identified 108 patients (50 male, 58 female, mean age 56.5 +/- 15.3 years) undergoing 90 fusions and 36 osteotomies at the level of the ankle, subtalar, Chopart or Lisfranc joint from January to December 2006. Thereby, 3 patients underwent revision of their arthrodesis within the follow up time. Another 15 underwent combined osteotomies or arthrodesis during the same procedure. Acellular allografts (Tutoplast®) and demineralised bone matrix (DBM) were the most often used structural and non structural bone graft respectively. Given the limited number of patients receiving the same graft in a specific procedure, comparison of time to union could only performed for structural and non structural bone grafts in triple/subtalar arthrodesis. In this category, there was no difference between acellular allograft mediated arthrodeses carried out either with or without DBM. Furthermore, there was no difference between in situ arthrodeses carried out without any graft or with the application of DBM.

Conclusion: Many different structural and non structural bone grafts and substitutes are used in fusions and osteotomies in today’s foot and ankle surgery for structural support or acelleration of bony healing. The current literature only provides sparse data on the efficacy of both natural bone grafts and their substitutes. Their true efficacy must further be evaluated in prospective randomized studies.

2. Introduction

Fusions and various realignment osteotomies of the ankle and the hindfoot implicate the decision whether to use or to abandon an autologous bone graft or a substitute material to either promote bony union and/or to additionally support the correction of a deformity. In opening wedge osteotomies and interposition arthrodesis, the surgeon has to choose between a structural bone graft and a substitute material for mechanical support and promotion of bone ingrowth in the resulting gap. In closing wedge and sliding osteotomies, there is the option to add cancellous bone or a substitute osteoinductive material to enhance bony union. The same option exists as an additive procedure to simple cartilage removal for in situ arthrodesis of the ankle and hindfoot. The abundance of different substitutes of structural and cancellous bone grafts available even multiplies the number of options in these decision making processes. This introduction should highlight the indications, properties and clinical results of structural and cancellous autologous grafts and their substitute materials in the context their application in fusions and osteotomies of the ankle and hindfoot.

2.1. Structural cortical bone grafts and substitutes

2.1.1.Indications, required and existing properties

Structural bone grafts and substitute materials are used in ankle and hindfoot arthrodesis to either replace degenerative or posttraumatic bone loss and/or to correct malalignment of the hindfoot. Thereby, the graft or substitute material is placed in between the joint space prior to fusion in terms of an interposition arthrodesis. Depending on the joint(s) fused, one may distinguish between isolated ankle, subtalar, talnonavicular or calcaneocuboideal arthrodesis and combined fusions such as double, triple and pantalar arthrodesis. Besides primary and secondary osteoarthritis [1] [2] [3] [4], the underlying conditions treated with interposition arthrodesis include end stage posterior tibial tendon insufficiency [5] [6], acute calcaneus [7] [8] [9] distal tibia fractures [10] and deformities associated with neuromuscular disease [11] [12]. In ankle and hindfoot osteotomies, the need for a structural bone replacement emerges whenever the correction of malalignment results in the creation of an open wedge. Such open wedge osteotomies include supramalleolar medial valgisation OT and lateral varisations OT [13, 14] to correct valgus and varus malaligment of the ankle joint respectively. On the level of the calacaneus, open wedge OT comprise lateral calcaneus lengthening OT to treat stage two tibial tendon insufficiencies [15-19] and medial opening Dwyer OT [20#] to correct varus malalignment of the calcaneus [20]. Since the ankle and hindfoot represents a mechanically challenging part of the skeleton, structural bone grafts and substitute materials used in the above mentioned conditions need to be resistant to external loading. Moreover, they should be made from a biocompatible, resorbable matrix providing rapid ingrowth of bone forming cells (osteoconductivity) leading to early transformation of the bone replacement into stable, natural bone. An additional content of osteoinductive growth factors supporting differentiation of intrinsic and invading cells into osteoblasts may be beneficial by further stimulating ossifaction of the bone gap. Autologous cortical bone grafts harvested from the iliac crest

or fibula used as a bone replacement provides most of these required properties. Upon transplantation, autologous cortical grafts are usually well incorporated [21-24]. Invading cells resorbe, vascularize and replace the graft by new bone [25#]. The process of resorption might additionally release some osteoinductive growth factors [26], but may also weaken the graft in the in the first six weeks upon transplantation. Indeed, the biomechanical properties are restored by six months, once the graft is replaced by new bone [27]. Yet, cortical grafts can be harvested with their vascular pedicle as a vascularized graft (e.g. from the fibula) and microsurgically connected to the blood vessels of the recipient site. Thereby, a certain amount osteoblasts and osteoprogenitor cells (such as endostal lining cells) survive inside the graft in contrast to non vascularized grafts which consistently display a necrotic core upon transplantation due to deprivation of oxygen and nutrient supply [23]. The surviving osteoblasts inside the graft - as well as their precursors after differentiation- are capable to form bone inside the graft constituting an additional osteogenic property of such transplants[28]. Since such vascularized grafts are incorporated by fusion to the recipient bone and not by resorption like non vascularized grafts, they provide even increased mechanical stability in the early period after transplantation [23].

Despite of the excellent properties of autologous cortical vascularized and non vascularized grafts, there are some drawbacks in clinical application including increased surgery time for graft preparation, limited availability and associated donor site morbidity [29-35]. Although the latter may be not as pronounced in foot and ankle surgery as reported in spinal surgery, it may still be considered as clinically relevant. De Orio et al [36#] reviewed 134 patients who underwent anterior iliac crest bone grafting for foot and ankle surgery during a 12 year period. 27% of these patients retrospectively reported that pain at the graft site was greater than at the surgical site and 6.7% showed local hematoma or seroma. Chronic pain or residual numbness at the harvest site was present in 10% of patients in this series. Such intrinsic disadvantages of autogenous cortical bone grafts opened the field to the currently growing number of substitute materials. Among those, fresh frozen and freeze dried allografts from tissue banks were first used in foot and ankle surgery. They are comparable to autologous cortical grafts in terms of osteoconductivity and possible osteoinductivity. But upon transplantation, they may incite an immunologic response [37, 38] and show delayed vascularisation [39, 40] leading to impaired incorporation [41, 42] and even secondary failure [43#]. Additionally, there is the risk of infectious disease transmission [44]. To lower the immunologic and infectious risk potential, techniques have been developed to wash cells and non collagenous proteins out of the allograft to convert it in a purely osteoconductive, mechanically stable matrix mainly consisting of collagen and hydoxyapatite [45]. As this matrix is considered to be immunologically inert, it can even be derived from xenografts (e.g. from bovine bone) [46]. However, mechanical resistance and osteointegration might still be inferior to autogenous grafts [47#]. Nevertheless, such anorganic allo- and xenoggrafts are currently widely used in orthopaedic and maxillofacial surgery [48, 49, 49, 50]. As an alternative to allografts and derived products, synthetic porous ceramic scaffolds consisting of hydroxyapatite (HA) and related calcium phosphates like α and β tricalciumphosphate (TCP) have been promoted as cortical bone graft substitutes. They promote bone ingrowth due to a specific configuration of ideally 90% porosity and 100 µm diameter [51,

[52]. The HA as well as the TCP surface has additionally been reported to promote osteoblastic differentiation of adhering osteoprogenitor cells [53#] . However, their distinct brittleness combined renders them unattractive for heavily loaded areas [54]. Moreover, particularly HA based ceramics degrade slowly[55]. Thus, bone gaps filled with HA based ceramics will achieve the same stability as the ones filled with natural bone significantly delayed.

2.1.2. Clinical results reported in the literature:

There are numerous retrospective studies investigating the use of structural bone auto- or allografts in subtalar and triple interposition arthrodesis and calacaneus lengthening osteotomies. Among these studies, several smaller series showed high union rates in subtalar interposition arthrodesis using iliac crest derived autografts: Amendola et al. [7] report on 100% unions (15/15) while Carr et al [3] and Bednarz et al [56] achieved union in 86-87% (13/15, 32/37 and 24/28 respectively). Excellent union rates were also achieved in small series using structural autografts in interposition triple arthrodesis and calcaneus lengthening osteotomies. In the series of Bednarz in 1999 [57], iliac crest bone grafts were used in 56 triple arthrodeses. Union was achieved in 52 patients (92%) with substantial and sustained deformity correction. Hintermann et al [15] reviewed 16 patients undergoing lateral calcaneus ostetomies among which 13 received autogenous iliac crest bone graft and three acellular allograft (Tutoplast ®). One year after surgery, all autografts were incorporated with continuous preservation of deformity correction. One acellular allograft showed early resoption and had to be replaced by an autograft 10 weeks after the primary surgery. Zwipp et al [19] reported on similar excellent results: There was only one non union in a series of 21 lateral calcaneus osteotomies using autogenous iliac crest bone grafts. The use of allografts in various arthrodesis and osteotomies was investigated in an extensive retrospective series by Myerson et al.[58] 75 operations were included ranging from ankle, tbiocalcaneal, subtalar, calcaneocuboideal, MTP and TMT interposition arthrodesis as well as lateral calcaneus lengthening, medial cuneiform and fibular osteotomies. 69 out of these 79 procedures (92%) were reported to be followed by successful healing. No graft failure was noted. However, time to union varied from 2-10 months and exceeded 4 months in 22 procedures (29%). Non- and delayed unions occurred in patients with revision surgeries, previous infections or substantial cigarette consumption.

There are some comparative studies comparing cortical and fresh frozen or acellular allografts. Most of them are retrospective. Easly and co-workers [59] reviewed 184 isolated subtalar arthrodesis including 34 procedures where interposition with a structural bone graft was required. In five out of these 34 cases fresh frozen allografts were applied while in the remaining 29 cases an autologous tricortical bone graft was used. There was non union in three out of the five (40%) patients receiving a structural allograft, while in only 17% of patients with structural autografts sustained a non union. However, the low number of patients included in this subanalysis and the retrospective study design diminish the validity of this comparative analysis. The use of allograft bone in hindfoot arthrodesis was also evaluated in a retrospective study by Mac Garvey et al [60] including a slightly higher number of patients. The authors analysed 41 hindfoot fusions (double, triple and subtalar arthrodesis) with the use of 27 allograft and 17 autograft structural bone grafts. There were more non unions in the allograft

group than in the autograft group (3/27 (11.1%) vs 1/17 (5.8%) respectively). Allografts have also been retrospectively been compared with autografts in three studies on lateral column lengthening to treat pes planovalgus deformity in children occurring idiopathically or in the context of cerebral palsy and other neuromoscular deformities. Kwak et al [61] reviewed 118 cases of lateral intracalcalcaneal lengthening carried out by the same surgeon in pediatric flat feet either using autogenous iliac crest bone graft (10 patients) or acellular allografts (Tutoplast ®, 108 patients). Regarding the correction of the previous deformity (as expressed by the calcaneal pitch as well as the talocalcaneal and talo-1st metatarsal angle) and union rate there were no significant differences between the groups. These results were also reproduced Templin [17]reviewing a smaller series of allo-and autograft mediated lateral column lengthening in skeletally immature patients. Danko et al [62] assessed if the correction of the flatfoot deformity can be maintained over time. They compared auto- and allografts used in 69 intracalcaneal lengthening procedures and 61 calcanealcuboideal arthrodesis . Though allografts provided equivalent results in intracalcaneal lengthening as compared to autografts after a mean follow up time of 2.5 years, significant increased allograft collaps was observed in calcanealcuboideal arthrodesis.

Auto and allografts were also retrospectively compared in a very heterogenic study population by Mahan et al [63]. They reviewed 300 foot and ankle procedures varying from arthrodesis to open wedge osteotomies and trauma cases in which a total of 217 allografts and 83 autografts were used. The authors could not observe any significant difference regarding delayed or non unions or other complications. According to our Dolan et al [64] compared the use of freeze dried cortical allograft (from a bone bank) with tricortical autograft in 31 patients (33 feet) with acquired flatfoot undergoing lateral column lengthening. At the eight weeks follow-up significantly more patients achieved union in the allograft than in the autograft group (94.4 % versus 60% respectively). Yet, at the twelve weeks follow up bony union was achieved in all patients both groups. Though it was a randomized and well conducted study, no power calculation was made to determine the number of patients necessary to detect a significant difference even in the long term follow-up.

2.2. Non structural cancellous bone grafts and substitutes

2.2.1. Indications, required and existing properties

The main purpose of cancellous bone grafts and substitutes is the promotion of bony union or to fill bone gaps in unloaded areas of the skeleton. Thus, in hindfoot arthrodesis it is used to promote consolidation of joints fused in situ, i.e. without any distraction by a bone block to realign the hindfoot. In these procedures, the addition of a cancellous graft or a substitute material is considered as an accessory procedure since the associated cartilage removal already exposes the underlying cancellous bone. But the surgeon may be tempted to add a cancellous graft or an equivalent material in those cases prone to non union. In the series by Easly et al [59] reviewing subtalar 184 arthrodesis, several important risk factors for non unions were identified: Smoking increased the risk of non union from 8% to 27%. Revision arthrodesis failed to heal in 29% while only 14% of primary arthrodesis

ended in a non union. The presence of avascular bone at the time of surgery raised the risk of non union up to 38% .The markedly increased risk of non unions among smokers was confirmed in the retrospective series by Chahal et al. [65] and Ishikawa [65, 66]reviewing 88 primary subtalar arthrodesis and 106 triple and subtalar arthrodesis respectively . In these series, the non union rate among smokers was 3.8 and 2.7 times higher as compared to non smokers. Moreover, Chahal et al [65#] observed a 18.7 times more non unions among diabetic patients as compared to non diabetic patients. In conclusion, the disposal of a cancellous bone grafts or a substitute material converts from an option into an important consideration in diabetic and smoking patients, revision surgery and in the presence of avascular bone. In hindfoot and ankle osteotomies, the application of cancellous grafts and equivalent materials is intrinsically limited to deformity corrections with a closing wedge or a translational displacement (sliding osteotomies). But, the utility is not so obvious since the main interface of such osteotomy gaps already consists of cancellous bone. Yet, cancellous grafts and substitutes could be an option in patients with poor local bone quality due to osteoporosis, diabetes and poor vascular status.

The acceleration of bony consolidation of ankle and hindfoot in situ arthrodesis and non distracting osteotomies requires the addition of a component providing major osteoinductivity and some osteoconductivity. Autologous cancellous bone, which can be harvested at various sites such as the iliac crest, tibia (Gerdy tubercle) and calcaneus, consists of an osteoconductive matrix to which osteoinductive growth factors are bound. It is hypothesized, that the osteoinductive growth factors are released, once the graft is resorbed by invading cells and replaced by new bone [26, 65]. Though the scientific prove of this theory is still outstanding. Moreover, osteoblasts and precursors residing in the periphery of the cancellous graft may survive upon transplantation providing an additional osteogenic component [67#] . Like for autologous cortical bone, the excellent biologic behaviour of autologous cancellous bone is opposed to associated donor site morbidity, increased surgery time and limited availability. Though, the harvest of cancellous bone is certainly less traumatic and time consuming than the removal of a cortical graft. As recently demonstrated [68] donor sited morbidity is even more reduced, if cancellous grafts are harvested from the ipsilateral proximal tibia.

Yet, various materials have been promoted as appropriate substitutes of cancellous grafts including fresh frozen and freeze dried allografts (already presented in the last section), demineralised bone matrix (DBM), bone morphogenic proteins (BMP-s) and ceramic granules.
As first shown by Urist in 1965 [69], decalcification of bone results in a powder, namely DBM, with distinctive osetoinductive properties due to contained growth factors known as BMP's. Since DBM is also rich in collagen, some additional osteoconductivity is presumed. The admixture of different biocompatible carriers turns DBM into putty or a paste with distinct biomechanical properties. Though derived from allograft bone, its associated disease transmission risk and immunogenic response is negligible [70-72]. Following the breaking finding by Urist, the numerous BMP's have been characterised [73#]. BMP s are polypeptides with a short half life and belong to the TGFß superfamily responsible for various differentiation processes in the muskuloskletal system. Besides inducing osteoblastic

differentiation of progenitor cells with variable osteogenic committent, BMP's have also been demonstrated to trigger players in hematopoietic differentiation [74, 75]. With the development of recombinant techniques, BMP 2 and BMP 7 (also known as OP-1) were realeased as commercially available drugs. A comprehensive in vitro study [76] demonstrated that BMP 2 might be one of the most potent osteogenic growth factor among the BMP family since it is capable to direct even undifferentiated mesenchymal stem cells into the osteoblastic lineage, while BMP 7 acts on more mature osteoblasts. Besides osteoinductive growth factors, synthetic ceramics in the form of granules have been suggested particularly for in situ arthrodesis. Yet, their lack of the important osteoinductive capacity possibly limits their use for these applications.

2.2.2. Clinical results reported in the literature:

According to our knowledge, the use of non structural bone grafts and substitutes has so far not been evaluated for hindfoot and ankle OT, but has been investigated for ankle and hindfoot in situ fusions, though predominantly in non comparative, retrospective case series. Various retrospective studies tried to assess the value of autogenous cancellous grafts or substitutes in patients who are not particularly at risk for non unions. Rosenfeld et al [77#] reviewed a consecutive series of 100 triple arthrodesis carried out in 96 patients with primary, secondary and rheumatoid osteoarthristis, neuromuscular deformities and posterior tibial tendon insufficiency. They could only observe 4 non-unions (4%) with a mean time to union of 5.1 months (range 3 to17 months). These results were comparable to other series in which autogenous bone grafts were used with non unions rates from 2-3% [57] . Therefore, Rosenfeld et al [77] concluded that bone grafts might be avoided in patients comparable to their study population. These results were in line with the series of Easly and co-workers [59]: Among the 184 isolated subtalar arthrodesis reviewed, cancellous autografts and allografts were added in 94 and 17 procedures respectively, while no graft or substitute was applied in 39 patients. In terms of union, there was no statistically significant difference between these groups with 82-87% of these procedures finally ending in complete healing with an average time to union varying from 11-13 weeks. Yet, when translating these results into clinical practise, the intrinsically impaired validity of retrospective data should be taken into account. The definite value of cancellous grafts or substitutes in hindfoot fusions will only be evaluated in prospective randomized controlled trials which are still outstanding. In two other, very small retrospective case series [78 79] the application of corraline hydroxyapatite to promote bony union of hindfoot fusions was investigated . Mahan [79] proved in twenty patients the applicability of this material in foot surgery. Coughlin et al [78] reviewed ten patients 6.5 to 6.9 years after triple or subtalar arthrodesis augmented with coralline hydroxyapatite and found only one non union. Interestingly, in all cases the ceramic was still present on plain radiographs at the time of follow up.

Moving from retrospective studies to more significant prospective comparative trials, we only hit on two studies assessing the utility of DBM. Michelson and Curl [80] compared demineralised bone matrix (DBM) to iliac crest bone grafts as promoters of bone ingrowth in patients undergoing triple and subtalar in situ arthrodesis. There was no significant difference in terms of non unions and time to union in these groups: In patients undergoing subtalar arthrodesis, union was achieved in the DBM

group and autorgraft group after 3.7 and 3.8 months respectively. In patients undergoing triple arthrodesis, time to union took 2.7-3.1 and 3.1-3.4 in the autograft group and DBM group respectively. Though this study was designed as a propective comparative trial, only a few patients were included in this study (37 in the DBM and 18 in the autograft group). According to the record, no power calculation was made. Thus, the study might have been underpowered to detect a significant difference. Moreover allocation to the treatment groups was based on the patient's choice introducing the risk of selection bias. Thordarson and Kuehn. [81] compared union rates of complex hindfoot arthrodeses either augmented with DBM or a combination of DBM and cancellous allograft. Again, no significant difference could be observed. Non union rates were 8% and 14% in the DBM and DBM-allograft group respectively. However, there is again suspicion that the study might have been underpowered because only 63 patients were included. Moreover, there was no random allocation to the treatment groups leading to possibly imbalanced comparison groups.

There are currently no comparative studies on the use of (recombinant) bone morphogenic proteins and ceramic granules for in situ arthrodesis and non distracting osteotomies of the hindfoot. The use of corraline hydroxyaptatite granules was analysed in two retrospective case series [78, 79].

3. Conclusion and scientific question of this thesis:

Many different structural and non structural bone grafts and subsitutes are used in fusions and osteotomies in today's foot and ankle surgery for structural support or acceleration of bony healing. The current literature only provides sparse data on the efficacy of both natural bone grafts and their substitutes. The goal of this thesis is to retrospectively quantify the use of structural and non structural bone grafts in the foot and ankle clinic of the university hospital of Basel over a 1 year period and to assess the time to union achieved with each different type of graft in specific hindfoot fusions or osteotomies carried out at the level of the ankle, subtalar, Chopart and Lisfranc joint.

4. Materials and Methods:

4.1. Patient enrolment and data recording

We retrospectively identified all patients who underwent fusions of osteotomies of the hindfoot (including the Lisfranc joint) from January 2006 until December 2006 using the in house electronic database "opdz" recording all surgical procedures carried out at the institution of the University Hospital of Basel. Patients were then allocated to four major treatment categories 1) ankle fusion and osteotomies 2) hindfoot (talonavicular, subtalar and triple) arthrodesis 3) calcaneal osteotomy and 4) midfoot arthrodesis and osteotmies. Within these major treatment categories, patients were then listed in further graft subgroups pooling patients who have either received none or the same structural and non structural bone graft or substitute material. Using plain radiographs and patient files, we then recorded the time to union and the presence of delayed and non unions of fusions/osteotomies performed in patients included in our series. Average time to union, rates of non and delayed union was calculated for each of the above mentioned subgroups and compared to each other within the respective treatment categories.

4.2. Statistical analysis

Data were recorded in Microsoft Office Excel® tables. Using standard algorithms provided by the program, mean values, percentages and standard deviations were calculated within the groups mentioned above.

5. Results

5.1. Patient population

We identified 108 patients (58 female, 50 male, mean age 56.5± 15.3 years) undergoing 90 fusions and 36 osteotomies at the level of the ankle, subtalar, Chopart or Lisfranc joint from January to December 2006. 3 Patients underwent revision of their arthrodesis within the follow up time. Another 15 underwent combined osteotomies and/or arthrodesis during the same procedure. **Figure 1 and 2** show the absolute number per type of included arthrodeses and osteotomies respectively.

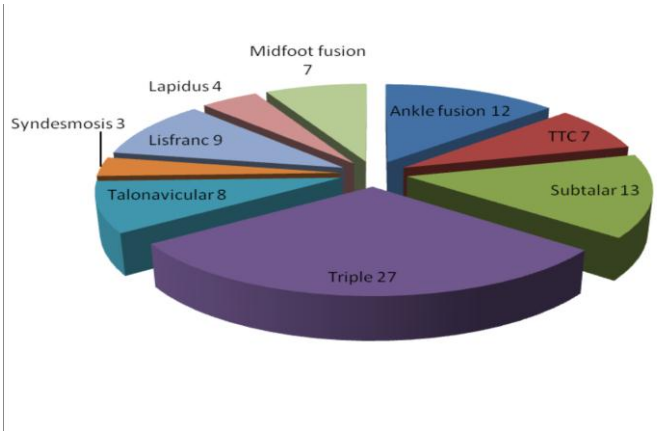

Figure 1: Distribution of the various types of arthrodeses included in the study. Values indicate the absolute numbers. Abbreviations: TTC = tibiocalcaneal arthrodesis

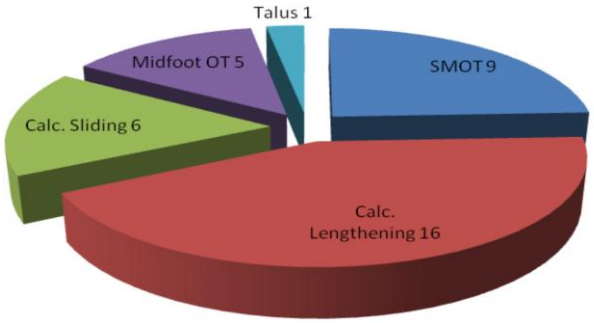

Figure 2: Distribution of various osteotomies included in the study. Values indicate absolute numbers. Abbreviations: Calc. length= Calcaneal lengthening osteotomy, SMOT= supramalleolar osteotomy, Calc sliding= calcaneal sliding osteotomy (medial or lateral).

32 out of total 126 (25.4%) procedures were revision cases. 57of the 108 patients included in the series (52.8%) showed at least one important co morbidity impairing bony healing such as presence of diabetes, smoking , medical treatment with steroids / methrotrexat and neuromuscular disease impairing the ability to perform protected weight bearing. Out of these 57 patients, 9 patients united 2 and 4 patients even three of these comorbidities. **Figure 3** shows the distribution of associated comorbidities.

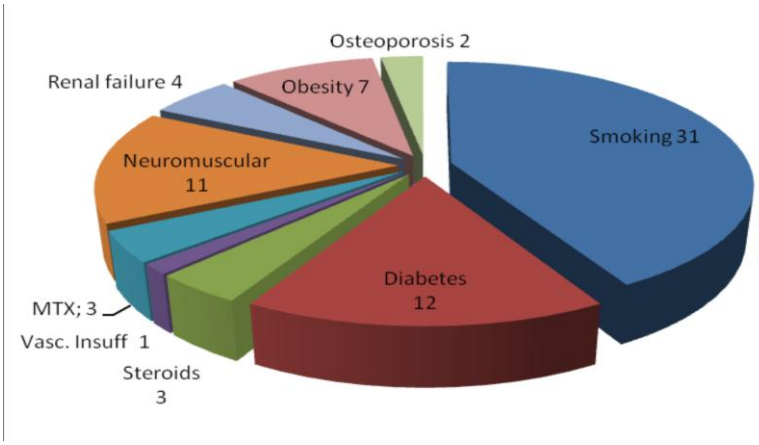

Figure 3: Distribution of various comorbidities of patients included in the study. Values indicate absolute number of patients per co morbidity. Abbreviations: MTX: treatment with Methotrexat, Vasc Insuff= Vascular insufficiency

5.2. Graft application

In 100 of total 126 (79.3%) osteotmies and arthrodeses included in the study, structural and non structural bone grafts were used. As shown in **figure 4**, structural grafts were by far the most frequently implanted grafts, followed by combined grafts (i.e. structural grafts augmented with an additional non structural graft, e.g. DBM). However, in arthrodesis all types of grafts were nearly equally used except for hindfoot fusions where structural and combined grafts were much more frequently used than others (**see figure 5**). In all types of osteotomies, structural grafts were the most predominant graft but many osteotomies were carried out without graft implantation. Combined grafts were never used for osteotomies (**see figure 6**).

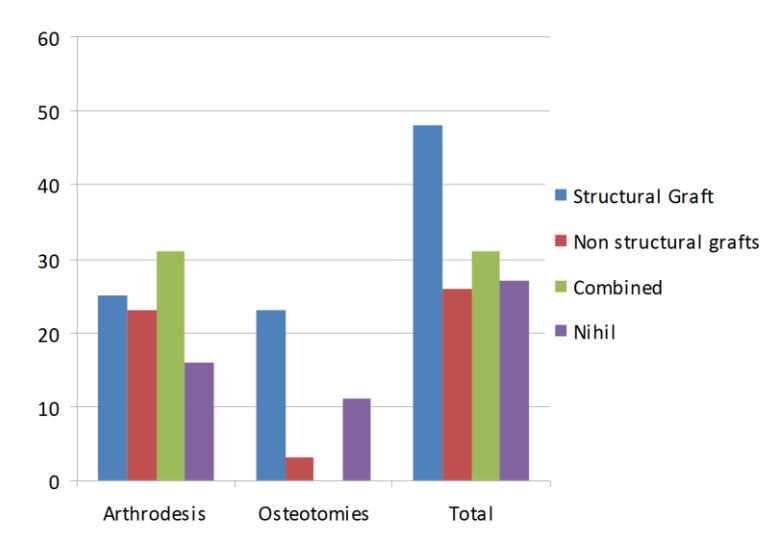

Figure 4 : Distribution of structural, non structural grafts and no graft used in the 126 osteotomies and arthrodesis included in the series.

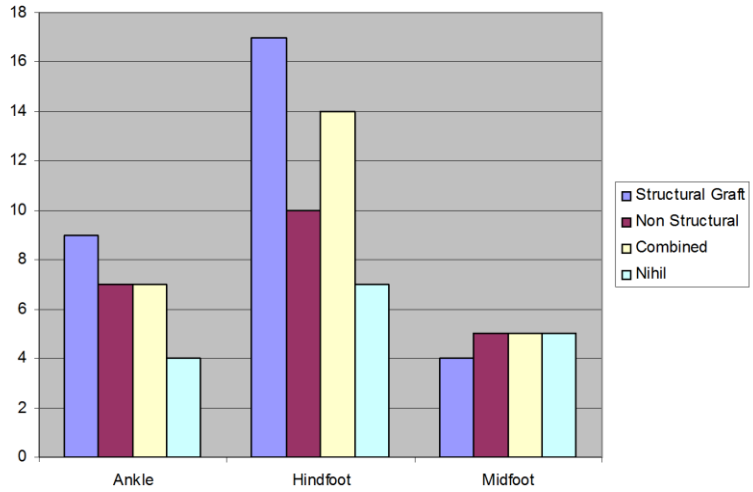

Figure 5: Distribution of structural, non structural and no bone grafts for ankle, hind-and midfoot arthrodesis included in the series. Ankle arthrodesis includes classic ankle fusion and tibio-talo-calnaeal fusions, Hindfoot arthrodesis includes triple, subtalar and talonavicular arthrodesis, midfootfusions include Lisfranc, naviculocuneiform and classic Lapidus arthrodesis.

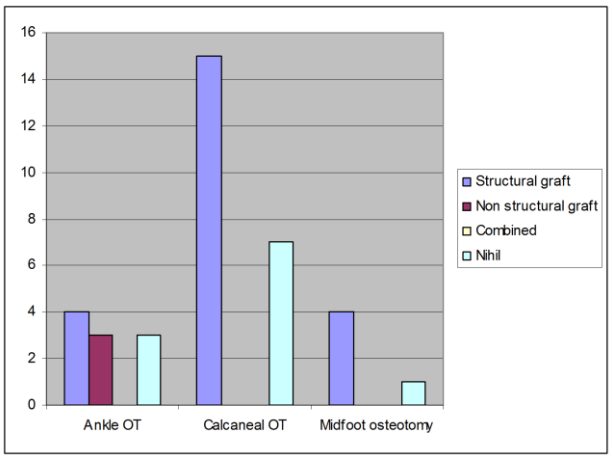

Figure 6: Distribution of structural, non structural and no bone grafts used for osteotomies included in the series. Values indicate absolute numbers Abbreviations: Calcaneal osteotmies include calcaneal lengthening osteotomy and calcaneal sliding osteotomies. Ankle osteotomies include supramalleolar osteotomies.

Among structural grafts, the use of acellular allografts (Tutoplast®) exceeded by far most the use of iliac crest bone grafts (89% versus 9%) in both arhrodeses and osteotomies (see figure 7, and figure 8 and 9). The most prominent use of Tutoplast® was noted in hindfoot fusions and calcaneal osteotomies (see figure 8 and 9) reflecting the high fraction of these procedures among the interventions recorded in this series.

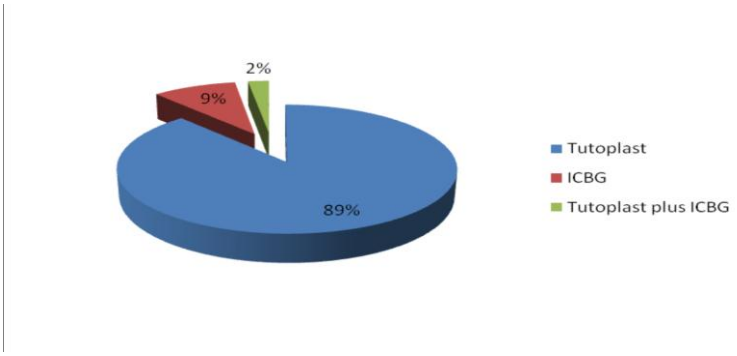

Figure 7: Overall distribution of structural grafts used. Abbreviation: ICBG= iliac crest bone graft

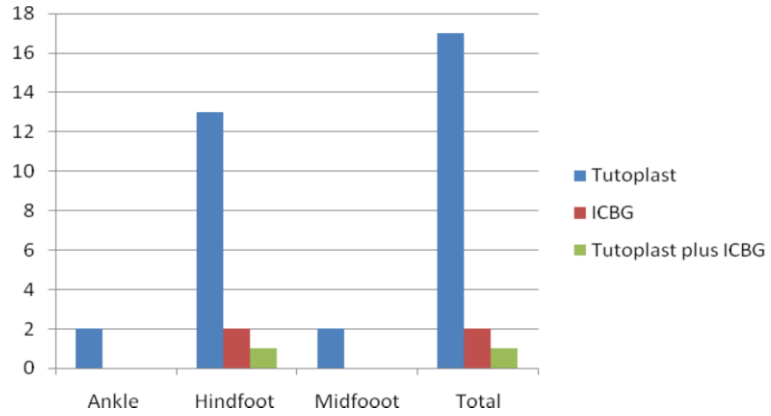

Figure 8: Distribution of structural grafts among the different types of arthrodesis. Figures indicate absolute numbers. Abbreviation: ICBG: iliac crest bone graft.

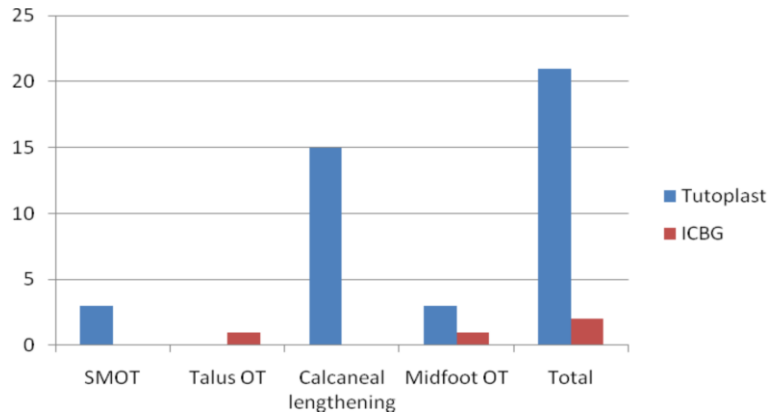

Figure 9: Distribution of structural grafts among different types of osteotomies. Abbreviation: SMOT: supramalleolar osteotomy, ICBG: iliac crest bone graft

Among non structural grafts, demineralised bone matrix (DBM) was clearly the preferred graft. Surprisingly, pure cancellous bone was only used in combination with DBM. Again the most prominent use of DBM was noted in hindfoot arthrodeses. In osteotomies, DBM and non structural grafts were only used in supramalleolar realignement procedures (see figure 10)

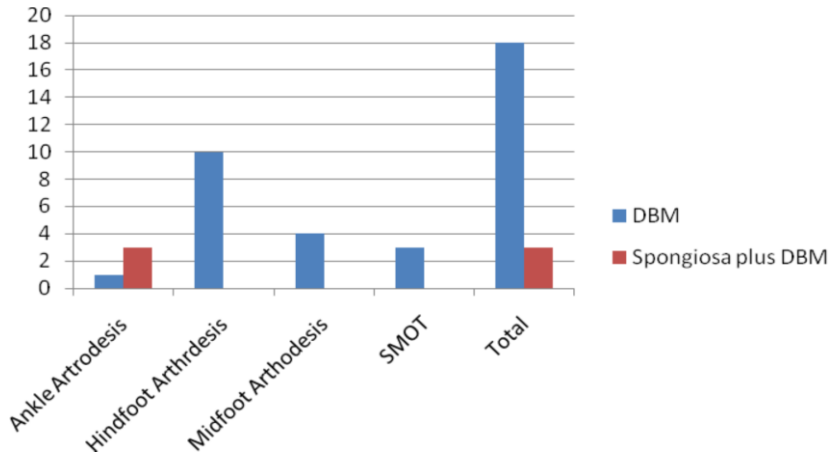

Figure 10: Distribution of non structural grafts in arthrodesis and osteotomies. Values indicate absolute numbers. Abbreviation: SMOT: supramalleolar osteotomy.

As already shown in figure 4, combined grafts (i.e. the combination of a structural or non structural graft) were only used in arthrodeses. The detailed analysis of combined grafts yielded a very heterogenic picture. Iliac crest bone grafts and acellular allografts were combined with all sorts of non structural grafts including even platelet lysate which was obtained from centrifugation of the patient's blood (see figure 11). However, Tutoplast® in combination with DBM was the most often used graft mainly in hindfoot fusions (see figure 12).

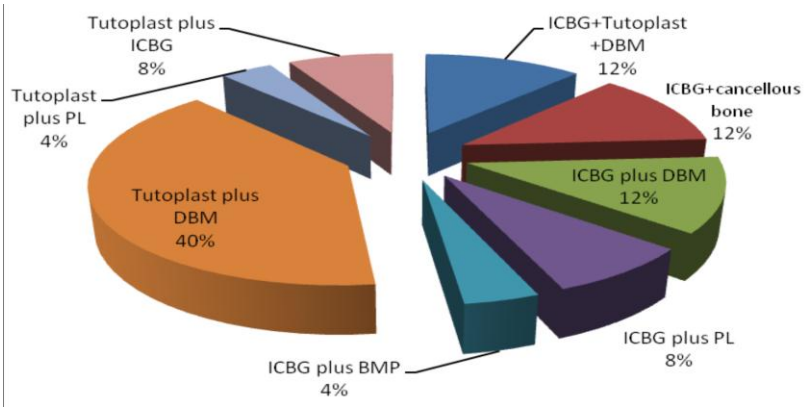

Figure 11: Distribution of the various combined grafts used in ankle-,hindfoot- and midfootarthrodesis. Abbreviations: ICBG= iliac crest bone graft, DBM= demineralised bone matrix, PL= platelet lysate.

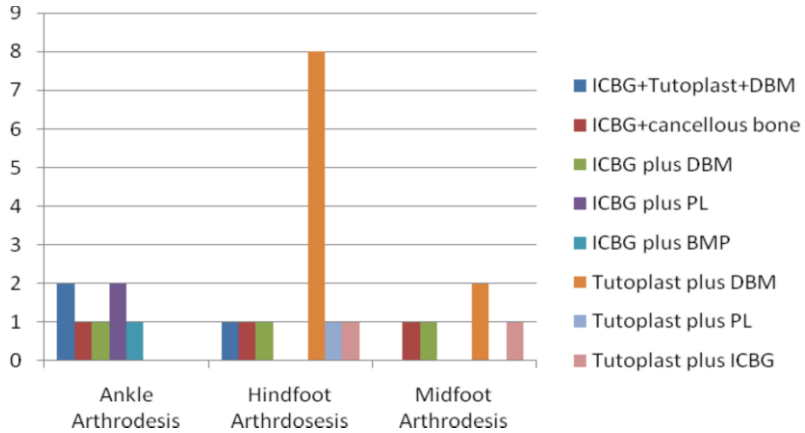

Figure 12: Distribution of the various combined grafts in the various types of arhrodeses. Values indicate absolute numbers. Abbreviations: ICBG= iliac crest bone graft, DBM= demineralised bone matrix, PL= platelet lysate.

5.3. Time to Union

In total, 102 out of.108 patients (94.4%) could be followed up over a period of 5.1± 1.5 months for evaluation of time to union and presence of delayed or non union respectively. 6 patients were lost to follow up (1 fusion of the syndesmosis, 1 tibiotalocalcaneal , 1 triple, 2 subtalar and 1 talonavicular arthrodesis). As shown in the preceding paragraph, the application of the various grafts was very heterogeneous making details analysis difficult. However, the following results are still worth being highlighted: Calcaneal osteotomies and interposition hindfoot arthrodesis performed with the application of Tutoplast ® showed similar time to union (figure 16) as compared to the healing times of these procedures reported in the literature[57, 82, 83]. Moreover, there was no graft collaps in the Tutoplast® group (data not shown). This may underline the utility of such acellular grats in hindfoot surgery. Furthermore, the addition of demineralised bone matrix to Tutoplast® did not significantly shorten healing times (figure 17). Similarly, there was no significant difference between healing times of in situ arthrodeses either performed with the application of no graft or with the addition of demineralised bone matrix (figure 13, 14 and 15)

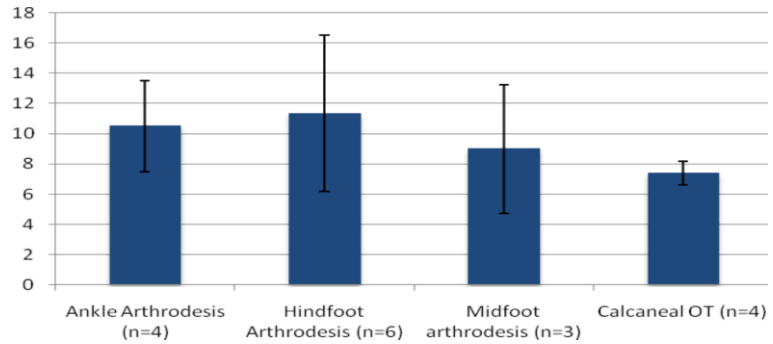

Figure 13: Time to union of ankle, hind-and midfoot arthrodesis and calcaneal osteotomies without application of any graft.

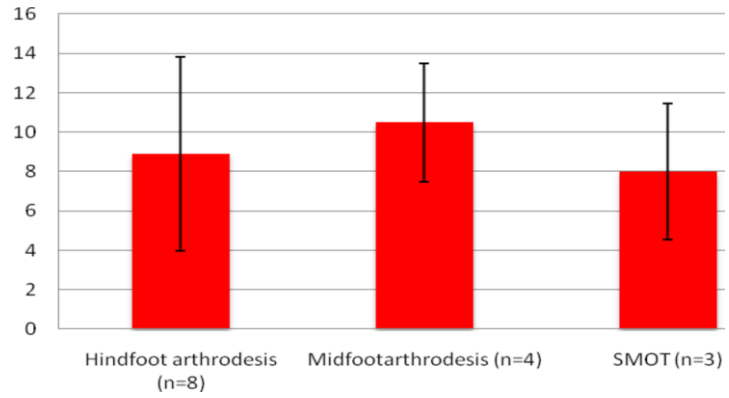

Figure 14: Time to union of various types of hind-,midfootarthrodesis and supramalleolar osteotomy with the application of demineralised bone matrix.

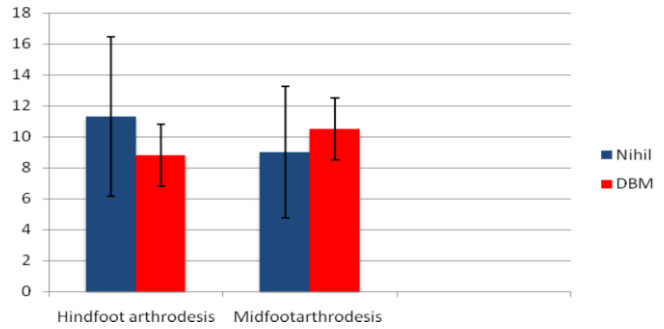

Figure 15: Comparison of time to union of hind-and midfootarthrodesis performed with either no graft or the application of demineralised bone matrix.

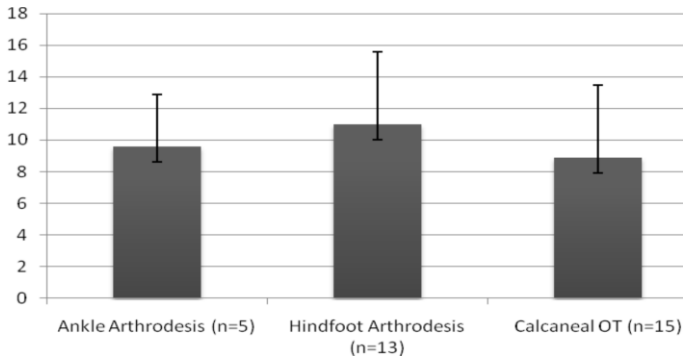

Figure 16: Time to union of ankle and hindfootarrthrodesis and calcaneal OT using acellular allograft (Tutoplast®)

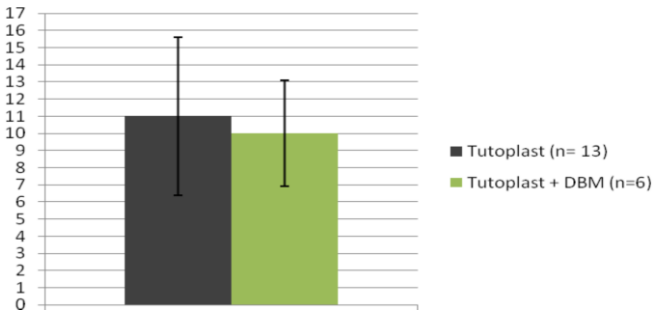

Figure 17: Comparison of time to union between hindfoot arthrodesis performed using acellular allograft with and without the addition of DBM

6. Discussion

The goal of this study was to retrospectively review the use of structural and non structural bone grafts and substitute materials used for hindfoot fusions at the foot and ankle clinic of University Hospital of Basel and thereby comparing average time to union achieved with specific grafts in specific hindfoot fusions. We identified 108 patients undergoing 90 fusions and 36 osteotomies at the level of the ankle, subtalar, Chopart or Lisfranc joint from January to December 2006. The use of bone grafts and substitute materials was very large. Almost 80% of our patients received bone grafts and substitutes. Although this frequency appears to be very high (especially for hindfoot arthrodesis), our results are comparable to others series [59#]. The analysis of the patient population showed that many patients showed at least one important co-morbidity impairing bone healing. Particularly, there was a substantial percentage of diabetic patients and smokers known to be at high risk to develop non union [59, 65]. This may explain the high percentage of grafts used.

Among structural grafts, the use of acellular allograft (Tutoplast®) exceeded by far the use of iliac crest bone grafts (89% versus 9%) in both arthrodeses and osteotomies. The most predominant use of Tutoplast® was noted in hindfoot fusions and calcaneal osteotomies reflecting the high fraction of these procedures among the interventions recorded in this series.

Among non structural grafts, demineralised bone matrix was clearly the preferred graft. Again, the most prominent use of DBM was noted in hindfoot arthrodeses. In the group of combined grafts, Iliac crest bone and acellular allograft were combined with all sorts of non structural grafts including even platelet lysate. However, Tutoplast in combination with DBM, was the most often used graft, again mainly in hindfoot fusions.

The analysis of time to union for all grafts in all types for arthrodeses or osteotomies was not possible because respective case numbers were very low. Bony healing for osteotomies and arthrodesis performed with Tutoplast was comparable to healing times of iliac crest bone graft mediated procedures as reported in the literature [57, 82, 82-84, 84]. Moreover, we did not identify any graft collaps with the use of Tutoplast, especially in calcaneal lengthening osteotomy (data not shown). Consequently, Tutoplast® appears to be a good bone substitute material in foot and ankle surgery, a fact that is not yet reported in the literature and needs further clarification in prospective randomized studies. Interestingly, the time to union in hindfoot arthrodesis was not accelerated if Tutoplast® was used together with a non structural graft such as demineralised bone matrix. This result is certainly in contrast to our expectations. Possibly, we could not show any difference because the number of patients included in these two comparative groups was very low. In contrast, comparisons of DBM against no graft showed accelerated time to union for procedures carried out with DBM in the subgroup of hindfoot arthrodesis. However, the difference was not significant because the time to union by hindfoot arthrodesis without graft was very variable showing a high standard deviation. Moreover, the time to union by midfootartrodesis without any graft was surprisingly short which may additionally question the real benefit of DBM.

This study was a retrospective study. In such studies, the patient population is very heterogenic and for that reason comparison between identified subgroups are very difficult. In our study, subgroups of

patient per graft and the type of operation were very small. Moreover, the patient population was very heterogenic in respect to co-morbidity and age. So it is difficult to compare these very different groups against each other. For these reasons, we have to interpret our results very carefully. The other problem of a retrospective study is that follow-up and postoperative treatments were not carried out in a standard manner. Both factors can influence the results. For example, if a patient's foot is immobilized longer in the postoperative period, chances of a union are much higher. With a very strict follow-up, we have the opportunity to diagnose the complications earlier (for example, a non union).

Furthermore, it is not sure if the electronic data bank of operations ("operationsdatenbank"=OPDZ) really represents all hind- and midfoot operations that were carried out in our study period. This system saves the operations in a computer exactly in the way the surgeon announced it preoperatively. When the surgeon did another intra-operative procedure, he may not have changed the description of his operation any more.

Despite the design of this retrospective study, we did a complete postoperative observation of various patients referring to union and non union. This was possible because the University Hospital of Basel is a center for foot and ankle procedures and the patients didn't wish to be followed up by any other doctor, possibly not as experienced in this field of orthopaedic surgery.

If we want to achieve better quality of the results presented in this thesis without changing the study design, it would be a good choice to expand the subgroup of hindfoot arthrodesis and calcaneal osteotomies carried out with Tutoplast®. These groups could then be compared with patients where the same operation was carried out with Tutoplast in combination with demineralised bone matrix or autologous iliac crest bone respectively. However, if we want to be absolutely sure which graft with which type of arthrodesis has the quickest time to union, we have to do a prospective randomized study. Such a study would need a high patient rate so that the difference can be shown. For this reason, such a study could only be done in a multicenter-setting.

7. Conclusion

In hindfoot arthrodeses and osteotomies, large volumes of bone grafts and substitute materials are used. In the year 2006, surgeons at the clinic of foot and ankle surgery of the University Hospital of Basel, predominantly used acellular allografts (Tutoplast®) for both osteotomies and arthrodesis. In arthrodesis, acellular grafts were very often combined with demineralised bone matrix, which probably does not accelerate bony healing. Generally, acellular alllografts were associated with bony union comparable to autologous bone, particularly in hindfoot arthrodesis and calcaneal osteotomies. In addition, we could not observe collaps of acellular grafts in our series. This may indicate that acellular graft is a good alternative to autologous bone in foot and ankle surgery. However, only a prospective randomized controlled multicenter trial will be able to clarify which type of graft will really provide shortest healing times and may reveal if current bone graft substitutes are really cost effective.

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