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Apert Syndrome: A Consensus on the Management of Apert Hands

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Introduction

Apert Syndrome is a congenital condition characterised by primary craniosynostosis, midfacial malformations and complex symmetrical malformations of the hands and feet. The hands demonstrate one of the most complex collections of congenital upper limb deformities, posing a significant challenge for the paediatric hand surgeon. This study examines the extant literature and current practice of the four UK specialist craniofacial units regarding the management of Apert hands in order to provide a basis for guideline development.

Methods

The current literature was reviewed. Survey-type questionnaires were distributed to the four UK specialist craniofacial units and responses analysed.

Results

Management of the Apert hand is largely dictated by the degree of malformation present. Although all units aim to achieve a five digit hand, variation in the timing of surgery, operative protocols and mobilisation policies exists.

Conclusion

The results of this study provide an interesting snapshot of the current management of Apert hands across the UK's specialist units. The four UK units remain congruent on most areas surrounding the management of Apert hands although some minor inter-unit variation exists. A multidisciplinary approach to management remains fundamental in optimising the regain of function and aesthetically acceptable hands.

INTRODUCTION

General Overview

Apert Syndrome (acrocephalosyndactyly type 1) is a congenital condition characterised by primary craniosynostosis, midfacial malformations and complex symmetrical malformations of the hands and feet (Water and Staecker, 2006) (Ko, 2016). The hands demonstrate a spectrum of disturbances across the soft tissue and bony structures and are one of the most complex collections of congenital upper limb deformities (S. J. Guero, 2005). The involvement of muscle, tendon and neurovascular bundles means the management of this multiple-malformation syndrome often entails numerous surgical procedures and poses a significant challenge to the paediatric hand surgeon (S. Guero et al., 2004). This review examines the extant literature pertaining to the management of hands in Apert syndrome and makes suggestions for both conservative and surgical management based on the available evidence, in addition to recommendations for further study.

Apert syndrome was first described in 1906 by French paediatrician *Eugene Apert* based on a study of nine patients (Freiman et al., 2006) and is a rare type craniosynostosis occurring in approximately 1:160,000 to 1:200,000 live births (Kaplan, 1991). The constellation of abnormalities including craniosynostosis (abnormal development and premature fusion of the cranial sutures), midface hypoplasia with retrusion and severe syndactyly (cutaneous and bony fusion) of the hands and feet means this complex condition is difficult to manage. Furthermore, psychomotor development may be delayed and a multidisciplinary approach to management is essential (Yacubian-Fernandes et al., 2005).

Apert syndrome is inherited either autosomal dominantly or, more commonly, as the result of a sporadic mutation, and is equally common in male and female populations (Fearon, 2003). The mutation involving two amino acid substitutions has been localized to chromosome 10, arm q; the site of the *FGFR2* (Fibroblast Growth Factor-2 Receptor) gene, which belongs to a complex intracellular signalling network controlling cell proliferation, differentiation, migration and survival in various contexts – notably cranial development and growth (Wilkie et al., 1995).

In addition to abnormal cranial and limb development, variable dysplasia in other skeletal regions and visceral abnormalities (including cardiac and gastrointestinal) have also been linked with the condition (Cohen and Kreiborg, 1993). The craniofacial abnormalities associated with Apert syndrome are clinically distinctive. Premature fusion of the coronal suture causes an acrocephalic (cone-shaped) head with a diminished antero-posterior diameter, flat occiput and a high prominent forehead⁹. Facially, midface hypoplasia, shallow orbits, proptosis, exophthalmus, a depressed nasal bridge, a prominent mandible, high-arched or cleft palate and crowded upper teeth may be observed (Kaplan, 1991) (Wakae et al., 2008).

Anatomy of the Hand in Apert Syndrome

The skeletal and soft-tissue hand abnormalities associated with Apert syndrome distinguish it from other types of acrocephalosyndactyly such as Crouzon syndrome. Common disturbances include complex syndactyly with bony fusion (involving the index, long and ring fingers), a short thumb with radial clinodactyly, symphalangism and simple syndactyly of the fourth web space (S. Guero et al., 2004).

A comprehensive description of the pathologic anatomy seen in the Apert hand has been reported by Upton (Upton, 1991), who classifies the syndactyly deformity by severity into type I, II or III. Anomalies of the intrinsic muscles, extrinsic tendons and neurovascular bundles are also seen within the soft-tissue structures (Holten et al., 1997). Upton's classification offers a comprehensive description of hand deformities and shall be used to guide surgical management based on the presence of a Type I, II or III deformity.

Type I

Also referred to as a *spade hand* or *obstetrician's hand*, this is the most common and least severe hand configuration (Upton, 1991). A shallow first webspace separates the thumb with radial clinodactyly and the index ray. The index, long and ring fingers form a mid-digital hand mass through a flat side-to-side union. This union is either a bony or cartilaginous and primarily exists at the metaphyseal level of the distal phalanx and the distal interphalangeal joint (the cartilaginous union commonly occurs between the index and long fingers). Longitudinal growth during the intrauterine period is not affected by this osseous union. The fourth interdigital space consists of a simple syndactyly with the distal interphalangeal joint well formed and functional. (See Figure 1 & Figure 2).

Type II

Also referred to as *mitten hand*, this type involves a more severe configuration with the thumb demonstrating a join via a simple complete or incomplete syndactyly to the index ray (without osseous union). The hand has a large, concave palm as a result of complex finger fusion at the distal phalangeal level. There is usually a complete, simple syndactyly in the 4th interdigital space. Most type II hands do however contain an adequate first web space. (See Figure 3).

Type III

Often referred to as the *hoof* or *rosebud*, type III represents the severest, although most uncommon configuration. A tight osseous or cartilaginous union is present between the thumb, index, long and ring fingers and all nail plates are conjoined – individual longitudinal ridges demarcating partial separation of the underlying distal phalangeal segments may be present. The fifth digit is spared from osseous union but joined by a complete, simple syndactyly. Synostosis of the fourth-fifth metacarpal is common. (See Figure 4).

A summary of the different types can be seen in Table 1.

Table 1: Upton's Classification of the Apert Hand (Upton, 1991)

Deformity	Type I	Type II	Type III
<i>Thumb radial clinodactyly</i>	Present	Present	Present
<i>Index radial clinodactyly</i>	Absent	Present	Present
<i>First web syndactyly</i>	Simple (non-osseous)	Simple (non-osseous)	Complex (osseous)
<i>Complex 2-3-4 syndactyly & symbrachyphalangism</i>	Present	Present	Present
<i>4-4 syndactyly</i>	Simple, incomplete	Simple, incomplete	Simple, complete

Management

This complex collection of anatomical malformations presents a significant challenge to the healthcare team and a multidisciplinary approach to management is essential to ensure maximal function is obtained. In order to optimise therapy, the degree of bony abnormality should be

ascertained through a comprehensive initial assessment following diagnosis of the condition (Fadda et al., 2015) (Xie et al., 2016).

The diagnosis of Apert syndrome is made on clinical grounds through identification of the features described above. Clinicians should be aware of a small number of associated anomalies that account for the majority of complications during the neonatal period (Kaplan, 1991):

1) Airway Patency

Respiratory distress may occur as the result of a malformed nasopharyngeal space (often compensated for by mouth breathing) (Xie et al., 2016).

2) Evidence for Central Nervous System Malformation

Kleeblattschädel deformities in particular should alert the clinician to consider the possibility of encephalocele, porencephaly, hydrocephaly or agenesis of the corpus callosum (CT scans are helpful in identifying such structural problems) (Breik et al., 2016) (Hevner, 2015) (Stark et al., 2015).

3) Oral Feeding Skills

Initially difficult due to intermittent mouth breathing and the configuration of the hard and soft palate, making suckling difficult (Pereira et al., 2009).

A repertoire of imaging modalities is available to assist clinicians in determining the degree of hand malformation present. Imaging with X-ray, three-dimensional Computed tomography (CT) and magnetic resonance imaging (MRI) has been reported in the literature to provide a successful and comprehensive assessment of the hand (Holten et al., 1997) (Holten et al., 1997) (Piza-Katzer et al., 2008) (Azouz et al., 1998) (Magid et al., 1991). X-ray alone provides a limited evaluation of the grossly abnormal anatomy, whereas CT and MRI are able to effectively demonstrate the soft-tissue anatomy in addition to the spatial arrangement of the bones (Holten et al., 1997).

Currently, most of the literature centres on the use of imaging modalities to assist with the prenatal diagnosis of Apert syndrome or for analysis of craniofacial morphology. Few studies examine the efficacy of imaging modalities to guide or determine the surgical management (and subsequent structural outcome) of the Apert hand, although their usefulness in delineating other hand disorders such as carpal bone fractures or cartilaginous defects has been demonstrated (Holten et al., 1997) (Azouz et al., 1998). (Holten et al., 1997) support the use of MRI to clearly delineate the complex anatomical disturbances present in Apert hands and believe it can impact positively on both surgical planning and operative duration.

Once the degree of hand malformation is determined, a surgical correction strategy can be planned, which is typically staged over a number of years. The most widely accepted time for initiation of surgical correction is when the patient is 6 months old (Fearon, 2003) (Zucker et al., 1991) although some centres advocate starting as early as 3 months (Guzanin et al., 2001) or as late as 9 months (Fearon, 2003) (Guero, 2005). Operative procedures generally occur at 6-month intervals with the consensus being that digital separation should be achieved by 3 years of age.

As patients with Apert syndrome have significantly limited hand function – often just a paddle to push objects rather than being able to grip or grasp – surgical intervention should be prioritised according to functional importance (Zucker et al., 1991). This will ultimately depend on the presence of thumb syndactyly and extent of soft tissue deficiency.

A broad first web space is important for ray function due to the short and often radially deviated thumb (Fearon, 2003). All type I hands (and most type II hands) contain an adequate first web space

which can be augmented via a number of techniques. These have been outlined in detail in the literature. Foucher et al. (Foucher et al., 2000) in their study of 67 first web space reconstructions (54 cases) concluded that the four-flap Z-plasty is an adequate technique for non-severe first web deformities and this remains one of the most commonly employed techniques (Fearon, 2003) (Zucker et al., 1991) (S. J. Guero, 2005) (Foucher et al., 2000).

In more severe cases; notably type III hands where there is a tight osseous or cartilaginous union between the thumb and index finger, Z-plasties alone are often insufficient (Zucker et al., 1991). In such instances, a dorsal flap can be used to provide the additional tissue required. The dorsal rotation-advancement flap is frequently used to line the first web space, based on its good coverage and avoidance of a skin graft (Fearon, 2003) (Zucker et al., 1991) (S. J. Guero, 2005). This technique, in addition to avoiding interdigitating flaps within the web space and scar tissue formation, has the added advantage of allowing subsequent surgical re-advancement to widen the web space (Fearon, 2003). Successful modifications of this flap have also been reported to broaden the apex of the flap and increase its length (Ghani, 2006).

The principles of syndactyly reconstruction are well established. The aim is to create functionally independent digits that are cosmetically acceptable for the patient and a “normal” web (Sherif, 1998). The prioritisation of border ray release is contentious (Fearon, 2003) (Zucker et al., 1991) (S. J. Guero, 2005) (Foucher et al., 2000) (Fereshtian and Upton, 1991). Upton, Zucker and Fereshtian prioritise the border rays. Fearon, who advocates releasing all 10 fingers (and toes) in a two-stage operative procedure, suggests that in order to create a five-digit hand, the first stage release should always be performed on either the ulnar or radial side of the central digit, to allow a complete release in two stages. If the border digits are released first (the index, long and ring fingers remain fused together), the remaining syndactyls can not all be released in the second stage without operating on both sides of the long finger – which may compromise its viability. Prioritising the release of border digits thus results in three operative procedures to create a five-digit hand rather than complete release in two stages (Fearon, 2003). Fearon also supports different web space separation on each hand during the first stage, followed by a second stage three months later to release all of the remaining interspaces.

Operative techniques used to separate the digits incorporate a variety of dorsal flaps, which can be proximally or distally based (Sherif, 1998) (“Dorsal Metacarpal Island Flap in Syndactyly Treatment : Annals of Plastic Surgery” 2016). The incision technique and skin graft preference differs between institutions. The options for incision are either zig-zag or straight-line. Zig-zag incisions, as popularised by Cronin (Cronin, 1956), Bauer et al. (Bauer et al., 1956), and Flatt (Flatt, 1962), remains the favoured technique of most surgeons (S. J. Guero, 2005) (Zucker et al., 1991) (Guzanin et al., 2001) (Quaba and Davison, 1990). Although a straight-line incision rejects most conventional principles of treatment, it is considered equally suitable by some surgeons (Fearon, 2003). The requirement to combine a dorsal flap with a skin graft may necessitate, however preference with regards to split-thickness or full-thickness grafts differs, as does donor site preference. Harvesting full-thickness grafts is operationally longer and has a lower success rate (“Dorsal Metacarpal Island Flap in Syndactyly Treatment : Annals of Plastic Surgery” 2016) but does not have the high incidence of secondary graft contracture associated with split-thickness skin grafts (Percival and Sykes, 1989). Split-thickness skin grafts will however allow for a larger surface area of graft to be obtained. Most surgeons opt for full-thickness skin grafts - usually from the lower abdominal flexion crease (S. J. Guero, 2005) (Fearon, 2003) (Chang et al., 2002).

Other notable studies include one by Lohmeyer et al. (2016) who adopted a two-stage operative protocol to treat 168 complex syndactyls. They considered the use of standard surgical techniques in this area to be limited, particularly where there is extensive bone fusion and taut soft tissue. They employed a two-stage operation comprising of progressive soft tissue distraction prior to syndactyly release, and reported that this led to improved aesthetic outcomes following fingertip remodeling.

Although considerable focus is dedicated to the first web space, Jung et al. (2012)(Jung et al., 2012) developed a reconstructive method to remodel the third web space. They utilized an *Integra*[®] (Integra LifeSciences Corporation, New Jersey, USA) dermal regeneration skin template(Dantzer and Braye, 2001), an artificial dermis, to reconstruct the left hand. In their case study, this was compared to the right hand, which was reconstructed using a conventional groin flap. They concluded that whilst both hands achieved similar outcomes, the use of the dermal skin template in the left hand did not require subsequent debulking procedures or as much peri-operative wound care.

The thumb is frequently involved in syndactyly and displays a severe radial clinodactyly at the MCP joint, which is often attributed to a duplication or an abnormal insertion of APB onto the radial aspect of the distal phalanx(S. J. Guero, 2005)(Fearon, 2003)(Upton, 1991)(Percival and Sykes, 1989). Treatment recommendations often prioritise the creation of a thumb to fashion a sufficient pinch mechanism between the thumb and index finger, and several authors(S. Guero et al., 2004)^{7,11,29,36} have described surgical techniques for doing so, including an initial corrective osteotomy of the delta phalanx³³. The timing of thumb osteotomy is usually between 2 to 4 years of age⁴(Fearon, 2003)(“Synostosis of the Ring-Small Finger Metacarpal in Apert Acro... : Journal of Pediatric Orthopaedics” 2016)(Oishi and Ezaki, 2010). Upton attempts to aggressively create the pinch mechanism and recommends combining a thumb lengthening open-wedge osteotomy with excision of the fourth-fifth metacarpal synostosis (whereby the harvest bone can be placed in the open wedge). This same-session technique is also advocated by Fearon. Van heest et al. recommend firstly determining the degree of radial deviation and whether a simple incomplete, simple complete or complete syndactyly with a delta phalanx is present. In type I deformities, where the thumb has a simple incomplete syndactyly, first web deepening will suffice. If there is a complete simple or complex syndactyly with a delta phalanx and marked radial deviation, a staged thumb correction is recommended to avoid potential vascular compromise during bilateral dissection of the thumb. The stages consist of first web space deepening (or creation) and an opening wedge osteotomy to correct the delta phalanx. Chang et al. report no complications of open or closed thumb osteotomies in their experience with 11 patients, and recommend intraoperative fluoroscopy to determine the exact osteotomy site. Oishi and Ezaki interestingly prefer to replace the traditionally employed Z-plasty incision, with a V-to-Y, Y-to-V flap design, highlighting its improved mobilisation of the skin and more aesthetically acceptable result. More recently, a technique utilising a pre-operative multi-slice computer tomography machine to assist in the operative planning has been developed. This operation corrects the deformity through a modified dome osteotomy of the proximal phalanx with soft tissue coverage from a bi-lobed flap.

The issue of necessity regarding thumb correction has been raised, however even if little is gained functionally, the cosmetic appearance achieved through good alignment is often important to both children and their parents³(Upton, 1991).

The pathologic anatomy of the nails has been well described by Upton and they are often less uniformly segmented in the hands than the feet¹¹. There is generally a common nail of the third, fourth and fifth digits, however the decisions regarding nail bed treatment are variable and largely underreported. Most centres opt not to use any special flaps for the purposes of nail bed recreation(Fearon, 2003). Although Upton considers paronychia flaps to be worthwhile and represent a subtle refinement in digit appearance(Upton, 1991). For adjustment of the nail plate itself, normal excision or electrocautery can be used (Fearon, 2003)(Upton, 1991).

Ray amputation was largely dictated by conventional practice and current consensus is that a full complement of 10 digits should be aimed for – Fearon did not perform any digital amputations in his series of 43 patients(Fearon, 2003) and together with Zucker et al.(Zucker et al., 1991), deem the ‘aesthetic significance of a five-digit hand to these children may be as great as the functional benefit of surgical correction’. The decision to proceed with ray amputation will be dictated by anatomical limitations.

Complications and secondary procedures should be expected owing to the complex hand anatomy. Guero et al. reported a revision rate of 21%, Barot and Caplan 18% and Chang et al 13% (S. J. Guero, 2005) (S. Guero et al., 2004) (Chang et al., 2002) (Van Heest et al., 1997). In Fearon's series of 43 patients, there were no major complications although minor complications included one re-exploration because of bleeding. 3% of his centre's syndactyls required subsequent operative release (Fearon, 2003). Functional complications of the thumb may also occur if it is significantly shortened as a result of the osteotomy (Oishi and Ezaki, 2010).

METHODS

To determine current management options for Apert hands, four specialist UK craniofacial units that routinely manage the condition were consulted through a survey-type questionnaire. For anonymity, each unit was randomly allocated a number from one to five (NB two surgeons managed the condition within a single unit).

To construct the descriptive cross-sectional survey items and maximise face validity, a phased approach was utilised that incorporated key items from the extant literature, consultation with field experts and an initial pilot of the questionnaire. This was refined prior to final distribution.

Due to the nature of this topic and the requirement for a unique sample (consultant level plastic surgeons who routinely operate on Apert hands), a non-random purposive sampling method was employed ("Research Methods in Health. Buckingham," n.d.). Hard copies of the survey-questionnaire were distributed to each unit via postal delivery and accompanied with a brief covering letter explaining the purpose of the research. Self-addressed envelopes were provided for completed responses.

RESULTS

The survey-questionnaire achieved a 100% response rate, with five surgeons across four craniofacial units completing it.

Age at initiation of hand surgery

Commencement of hand surgery was predominantly influenced by craniofacial operations, and to a slightly lesser extent, the type of hand present. The ages at which surgeons initiated surgical correction started from as early as 5 months in Unit 5. Unit 4 specified an age range of 6-to-9 months to allow for craniofacial operations whilst still reducing deformity and Unit 5 specifically stated 5 months onwards for a type III hand. Unit 1 opts to reconstruct the thumb at 6 months to suitably align with the craniofacial sequence. Unit 2 qualified their decision to commence surgery at 9 months through desirable patient hand size, anaesthetic clearance and the requisite for several procedures. Unit 3 specified an age range of 12-18 months (but commented that they would sometimes start before this to the release the thumb). See Figure 5.

First priority

There was a uniform consensus across all four units that the thumb should take first priority for Apert hand reconstruction. Unit 4 however did differ slightly, by opting to separate all digits during the first operation and focus on the thumb in the second operation in order to achieve five-digit hands in the least number of operative sessions. In the other four units, subsequent prioritisation after the thumb also remained largely uniform, with surgeons agreeing that reconstruction of the 4th web space should be the subsequent focus, with the overall intention of achieving a five-digit hand.

Operative aspects

With regards to the number of operations typically performed per hand, this ranged from 2 performed by Unit 4 (one to separate all fingers and one to correct thumb alignment/revise web spaces), to 2 or 3 by Unit 5, and 3 or 4 at both Unit 1 and Unit 2 (*see* Figure 6). Again, this was type dependent. Unit 3 did not specifically state the number of operations performed (and is excluded from Figure 6) but agreed the number varied on type. The decision to operate on both hands in the same operative sessions also varied slightly amongst units, with Unit 1 and Unit 5 not operating in the same operative session compared to Unit 4, Unit 2 and Unit 3 who opted to do so.

Web space reconstruction

For reconstruction of the web space, a flap was the preferred method of reconstruction across all units. Unit 1 specified that they used a *Jumping Man* or dorsal flap with a full-thickness skin graft. Unit 2 also specifically stated that they use a dorsal flap with a full-thickness skin graft.

Radial deviation of the thumb

For the treatment of radial deviation of the thumb, all units currently choose to perform an osteotomy as follows:

Table 2: Management of Radial Deviation of the Thumb

Unit	Osteotomy	K-Wiring	Bone Graft
1	✓	✓	
2		✓	✓
3	✓	✓	
4	✓	✓	
5	✓	✓	

Unit 3 also stated that they would occasionally leave the thumb alone for functional reasons, depending on the stiffness of the other digits.

Dressing & mobilisation

When considering dressing and mobilisation protocols, there was considerable variation amongst units in the specific dressings used. Unit 1 opt for a two-week immobilisation period in a *Cavicare* (Smith & Nephew, Australia) dressing. Unit 4 and Unit 2 use *Jelonet* (Smith & Nephew, Australia), gauze and either 'wool and a crepe bandage' or '*Velband* (BSN medical, Australia) and a crepe bandage' respectively. Both Unit 1 and the Unit 5 aim for normal hand mobilisation at the 2-week point and Unit 4 also splint the first web space for three months at night. Unit 2 opts to immobilise for slightly longer – 2.5 weeks – and then recommend free mobilisation. Unit 3 use a 'baby straightjacket' for 2-3 weeks and then remove this to facilitate mobilisation.

Craniofacial service

All four units responded similarly when considering interaction with their respective craniofacial service. This included the implementation of a peripheral member sited on the multidisciplinary team, the employment of craniofacial co-ordinators, parallel clinics and craniofacial liaison nurses who work alongside the hand surgery team. All units reported that craniofacial surgery takes priority over hand surgery.

DISCUSSION

The results of this study provide an interesting snapshot of the current landscape pertaining to the management of Apert hands across the UK. Although all units aim to achieve a five-digit hand, variation in the timing of surgery, operative protocols and mobilisation policies is prevalent.

There is an interesting variation in the age range for which surgeons are prepared to initiate surgical correction. All respondents agreed that this largely depended on the craniofacial aspects of surgery, although the reported patient ages to initiate surgical treatment ranged from 5 months to 12 months. The rationale for commencing surgery earlier included deformity reduction and the type of hand present – e.g. a type III hand underwent surgery at 5 months. Later operative management may be dictated by the complexity of preceding craniofacial surgery or the type of present. Additional points for consideration included starting surgery at 9 months, whereby the hand is of a more desirable size to operate on and the patient is at a more preferable for anaesthetic purposes. Considerable variation around age for the initiation of surgical management is also apparent in the extant literature (*see Figure 7*):

The findings of this study concerning patient age are aligned with other international units, including those in the USA, Canada and Europe (*S. J. Guero, 2005*) (*Fearon, 2003*) (*Zucker et al., 1991*) (*Guzanin et al., 2001*) (*Chang et al., 2002*). Several authors have also described their rationale for performing hand surgery early; Holten et al. have emphasised how motion can facilitate preservation of the atypical joints seen in Apert hands whilst Upton has suggested that postponing surgery may result in delayed development and impaired body image (*Holten et al., 1997*). Barot and Caplan's (*Barot and Caplan, 1986*) 1986 paper also advocated early surgical intervention to minimise progressive growth deformity, which supports the findings of this study.

With regards to formalisation and subsequent adoption of a management protocol, the age to initiate surgical correction does not need to be definitively narrow. It is apparent from both this study and those examining practice outside of the UK that patients should be considered on an individual basis and priority given to the craniofacial aspects of a patient's surgery.

Although this study reveals some variation regarding patient age at the time of surgery, this does not in any way distract from the thumb remaining as first priority. Three of the units responded with the thumb as their first reconstructive priority, owing to its ability to facilitate opposition, which is of principal functional benefit to the patient. The secondary priority was a fourth web space release to allow function of the little finger. One unit purposely separated all digits within the first operative session to create a five-digit hand and focused on thumb alignment (and any necessary web revision) in a second operative session to minimise the overall number of operations.

The reconstructive goals highlighted above are synonymous with those described in the current literature (*Chang et al., 2002*) (*Gupta et al., 2000*), however, the number of operative sessions required to achieve such goals varied. Completing surgical management in the least number of sessions is generally preferable as this reduces total anaesthetic time and physiological disturbance, and also the psychosocial impact surgery may have on patients and family members. Studies have also indicated that a high number of general anaesthetics at a young age can result in decreased intellectual capacity (*Fadda et al., 2015*). This must be considered in a risk: benefit evaluation against the desirable outcome of a functioning five-digit hand, but will also be influenced by the anatomical complexity of the hand at presentation. Guero et al. (*S. J. Guero., 2005*), in their proposed treatment algorithm for Apert hands, seeks to achieve a five-digit hand in a 3-step procedure, operating bilaterally during the first procedure (to open the first and third web spaces and correct the thumb without osteotomy) and then operating on each hand individually at 6 month intervals to separate the second and fourth web spaces. This algorithm is however only followed for Upton Type I and II hands. For Type III deformities, the algorithm advocates removal of the fourth digit, which conflicts with current UK practice.

With regards to reconstruction of the web space, all units opted to employ a variant of flap, including *Jumping Man* and *dorsal* flaps. Dorsal flaps, such as the one described by Buck-Gramcko (S. J. Guero, 2005), provide good coverage and may avoid additional skin grafting. Where necessary, the units surveyed in this study used full-thickness skin grafts to achieve soft tissue coverage. This practice is also consistent with international units; Chang et al. highlight the effectiveness of local flaps and full thickness skin grafting (reporting a 13% revision rate), as do Guero et al. (15% revision rate) (S. J. Guero, 2005) (Chang et al., 2002). Flap and skin graft combinations are likely to remain as the central reconstructive options based on their clinical and cost-effectiveness, particularly in comparison to more time-consuming and costly options such as tissue expansion and Silastic sheeting (Coombs and Mutimer, 1994) (Stefansson and Stilwell, 1994).

The decision to operate on both hands during the same operative session varied. Operating bilaterally in the same session may reduce the total number of distinct operations required, but necessitates a recovery period where both upper limbs are immobilised. Bilateral limb immobilisation may well be more distressful for a child (and parents) in comparison to unilateral immobilisation. This however may outweigh the inherent risk of additional operations if a similarly functioning five-digit hand can be achieved. Indeed, some authors are strong advocates of operating bilaterally – Fearon et al. favour the release of all 10 fingers (and toes) in two operative sessions (Fearon, 2003). This decision will again be contingent on the complexity of the deformity present and the surgical feasibility of bilateral operations.

For thumb reconstruction specifically, all units operated using an osteotomy. Two units specified that they used an open wedge osteotomy - one with bone graft and one without. In both this study and internationally, an open wedge osteotomy appears to be used in preference to a closing wedge osteotomy (S. J. Guero, 2005) (Fearon, 2003) (Sherif, 1998) (Van Heest et al., 1997) (Chang et al., 2002) (Oishi and Ezaki, 2010). As an alternative to osteotomies and based on anatomical descriptions by Fereshetian and Upton²⁶, Dao and Wood⁴² promote the release of the long lever arm of the abnormal APB, which they deem responsible for the radial angulation of the thumb. This practice has been adopted over conventional osteotomy by some units (S. J. Guero, 2005). Although APB release is an apposite alternative, its advantages are unlikely to transform current UK practice, owing to the robustness of early osteotomy procedures and their negligible revision rates.

This study did highlight some differences in dressing and mobilisation protocols and largely concerned the choice of dressing used. Dressings play a critical role in a patient's recovery patients, helping to mitigate graft compromise through maceration and subsequent surgical revision. The majority of the UK units opt for gauze dressings that separate the digits, accompanied by a bulky dressing and crepe, and avoiding plaster immobilisation. Other options included the *Cavi-care* system, which is a conforming foam dressing. Dressing protocols are likely to be influenced by surgeons' experiences, preferences and patient satisfaction. Some institutions opt for cast immobilisation (usually above elbow), although there is little demonstrable evidence that this confers any benefit over simpler dressings or *Cavi-care* products with regards flap or skin-graft loss. Factors such as comfort, convenience and cost are also likely to govern the dressing decisions.

Most units, including those in this study and internationally, adopt a 2-to-3 week immobilisation period. Some institutions elect to change the first dressing after 8 days and then more frequently until complete healing is achieved (S. J. Guero, 2005), simply leave casts on for the entire 2-to-3 week period with or without subsequent customised splinting (Fearon, 2003) (Sherif, 1998) (Van Heest et al., 1997) (Oishi and Ezaki, 2010). Changing dressings may be more desirable in countries with warmer climates to reduce the impact of hyperhidrosis, which is present in most Apert patients (S. J. Guero, 2005).

Beyond the actual hand surgery itself, each of the four UK specialist units appear to work intimately with their respective craniofacial service, which is unsurprising due to the multidisciplinary nature of management each patient necessitates. As evident from the literature and results of this study, craniofacial surgery has a substantial impact on the timing of hand surgery and all units prioritise

craniofacial procedures. Although variation exists as to how craniofacial services are integrated, each unit acknowledges the importance of a hybrid service and a dedicated role to facilitate this.

Considerable effort is being put into driving the expansion of managing Apert Syndrome in resource poor nations. International partnerships between surgical units, such as those between Poland and North America, have successfully employed such models (Swanson *et al.*, 2016) and continue to work towards overcoming notable challenges, including the provision of training for local surgeons, optimisation of limited resources and cultural differences amongst members of the multi-disciplinary team.

In the longer-term future, the manipulation of genetic pathways may be a viable technology. Apert's Syndrome predominantly involves one of two sporadic missense mutations (in the FGFR2 exon 7) and consequent enhanced differentiation of osteoblasts (Wilkie *et al.*, 1995) (Yu *et al.*, 2000). A number of gene therapy approaches are seeking to modify these critical genetic pathways (Yin *et al.*, 2008) (Shukla *et al.*, 2007) (Holmes, 2012), with some success in inhibiting osteoblast differentiation (Suzuki *et al.*, 2012). However, the translation of this basic science research into the clinical setting remains distant and is complicated by the need for candidate therapeutics to be administered during foetal gestation. Current research applications also predominantly focus on the craniofacial aspects of Apert Syndrome and further work is required that specifically targets hand abnormalities (Gonçalves Leite *et al.*, 2015).

CONCLUSION

As evident from this study, UK units remain congruent on most aspects of Apert hand management. Minor inter-unit variation exists with regards to patient age at the initiation of surgery, the number of operations performed per hand, the decision to operate bilaterally within the same operative session and dressing protocols.

Further evaluation is required to establish the optimal time frames for key anatomical variants and the total number of operative sessions. General consensus exists with initiating surgical management early although the timings vary secondary to the influence of craniofacial procedures. All UK units are in agreement that a five-digit hand is the primary reconstructive objective and employ operative techniques that are consistent with achieving this goal. Focus should now move to streamlining operative sessions and minimising the number of distinct procedures. An evidence-based approach should also be utilised to determine optimal immobilisation periods and the impact of when surgery is initiated on functional outcomes. To facilitate this, an exemplar protocol has been included in the appendix of this study and can assist units in auditing individual elements of their management sequence. Direction should also be extricated from craniofacial management algorithms and their consistent use of advanced imaging modalities for surgical planning and projecting morphological outcomes. This, alongside a complimentary base of genetic research and expanding international efforts will support patients in receiving efficacious and accessible healthcare.

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Conflicts of Interest

Conflicts of interest: none

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Illustration Captions:

Figure 1: Type I (dorsal view)

Figure 2: Type I (volar view)

Figure 3: Type II (volar view)

Figure 4: Type III (volar view)

Figure 5: Patient Age Range at Initiation of Surgical Correction

Figure 6: Number of Operations Performed per Hand

Figure 7: A Global Perspective on Patient Age for the Initiation of Hand Surgery

ACCEPTED MANUSCRIPT













