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Clinical Report

Osteogenesis Imperfecta: Phenotypic and Intraoperative Findings Observed in Patients Treated Surgically at the World Hearing Centre

Henryk Skarżyński, Kamila Osińska, Piotr Henryk Skarżyński

Institute of Physiology and Pathology of Hearing, World Hearing Center, Warsaw, Poland (HS, KO, PHS)
Department of Heart Failure and Cardiac Rehabilitation, Medical University of Warsaw, Warsaw, Poland (PHS)
Institute of Sensory Organs, Nadarzyn, Poland (PHS)

ORCID IDs of the authors: H.S. 0000-0001-7141-9851; K.O. 0000-0001-9738-5143; P.H.S. 0000-0002-4978-1915.

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OBJECTIVES: Osteogenesis imperfecta (OI) is a systemic connective tissue disease that affects many systems and organs. Features of the disease are bone deformities, blue sclerae, and changes in the teeth, all of which may be accompanied by hearing loss. Bone fragility also affects structures of the ear, with half the patients developing changes in the auditory ossicles, which manifest as hearing loss. The most typical malformation affects the stapes, although the site of malformation within the middle ear varies. This study aims to characterize patients with OI who underwent surgery due to hearing loss and to find factors that affect the hearing results.

MATERIALS and METHODS: This study presents an analysis of phenotypic and intraoperative changes among 20 patients with OI, treated surgically for hearing loss.

RESULTS: Hearing loss typically affects type I patients with OI. The most common changes concern stapes footplate, arms, and tympanic cavity lining. During reoperations, osseous regrowth was typically detected.

CONCLUSION: The greater the changes induced systemically by OI, the greater the risk of significant malformations in the middle ear. Patients with OI are at an increased risk of needing revision surgery and of suffering intraoperative complications such as bleeding, which hinders safe completion of the procedure.

KEYWORDS: Osteogenesis imperfecta, hearing loss, phenotype

INTRODUCTION

Osteogenesis imperfecta (OI) is a genetically conditioned connective tissue disorder that affects multiple systems and organs with a high collagen content. The most typical symptoms of the disease include increased bone fragility, excessive skin and joint laxity, dentinogenesis (abnormal tooth development accompanied by increased susceptibility to caries), as well as blue sclerae [1]. Approximately half of patients suffering from OI develop hearing loss, usually of the conductive type, caused by pathology within the middle ear. The commonly accepted classification of OI established by Sillence in 1979 [1] provides four basic types of the disorder, and it is based on the patients' phenotypic traits. It embraces OI type I, the mildest form of the disease characterized by blue sclerae and no bone deformities; type II, perinatal and lethal; type III, which is extremely severe at birth, followed by bone deformities arising from recurrent fractures during life; and type IV, which is moderately severe, with varying degrees of bone deformities and unchanged sclerae.

According to Kuurila et al. [2], OI type I is the most common form of the disease. Globally, studies report that 73% to 92% of all patients with OI are type I [2-6].

The most common pathologies affecting the ear are, as described in the available literature, immobilization of the stapes, as well as a thickened and fragile footplate, accompanied occasionally by obliteration of the oval window niche. Underdevelopment of the stapes crura and crural fractures are reported as well. There are also cases of pathology of the first or second ossicles, leading

Corresponding Address: Kamila Osińska E-mail: osinska.kam@gmail.com
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to immobilization of the epitympanum. Typically, there is increased vascularity of the lining of the tympanic cavity, which can often lead to severe bleeding during surgical maneuvers performed in the cavity [2, 5-12].

Santos et al. [13] provided further findings of ear abnormalities in patients with OI. Histopathological examination of temporal bones from OI type I cases showed that changes were most common in the niche of the oval and round windows-the stapes was often abnormal, and there was a separation between the stapes crura and the footplate. Partial obliteration of the scala tympani, with accompanying degeneration of the organ of Corti and stria vascularis, was also common.

This study aims to characterize patients with OI who underwent surgery due to hearing loss and to find factors that affect the hearing results.

MATERIALS AND METHODS

The study enrolled 20 patients, 11 males and 9 females, diagnosed with OI and hearing loss, treated at the World Hearing Centre of the Institute of Physiology and Pathology of Hearing. Eighteen subjects underwent surgery for hearing loss, 15 of whom were operated on solely at the Institute. Three of the study subjects were treated surgically before the age of 18, with two of the procedures performed exclusively at the Institute of Physiology and Pathology of Hearing. Tables 1 and 2 list details of the study group.

Table 1. Patients with osteogenesis imperfecta treated at the Institute of Physiology and Pathology of Hearing

Patient	Sex	Age at First Surgery
OI 1	M	17*
OI 2	M	14
OI 3	M	32*
OI 4	M	25
OI 5	F	61
OI 6	M	63
OI 7	F	32
OI 8	F	30
OI 9	F	17
OI 10	M	49
OI 11	M	37
OI 12	M	16*
OI 13	F	23
OI 14	M	27
OI 15	M	20
OI 16	M	22
OI 17	F	56
OI 18	F	45
OI 19	F	/–/
OI 20	F	/–/

* surgery performed outside the Institute of Physiology and Pathology of Hearing
/–/ no surgery performed
OI: osteogenesis imperfecta; M: male; F: female

The patients were scheduled for follow-up visits and were classified, according to Sillence [1], on the basis of their phenotypic traits (Table 2). The next step was to evaluate the surgical protocols of all the patients who had undergone surgical procedures due to hearing loss. All the surgeries were performed by the most experienced surgeon. The analyzed intraoperative factors were the following: ossicles involvement, if pathology concerned stapes, the part (footplate or arms) that was changed, tympanic cavity thickened lining occurrence and tendency to bleeding, whether staged surgeries were indicated, and also the causes of reoperations.

RESULTS

All patients included in the study had blue sclerae. Half the subjects showed excessively lax joints; lax skin was observed in 42% of patients. Dentinogenesis was reported in 50% of the subjects. The stature ranged from short to tall (102-178 cm). All patients had a history of numerous fractures of the long and short bones, as well as vertebral and pelvic fractures, ranging from 10 to 120 per patient. The mild form of the disease, OI type I, was the most common type (Table 2).

In terms of surgical observations, the most common changes seen at first surgery were the immobilization of the stapedial footplate, thickening of the stapes footplate by up to 2-3 mm, footplate fragility and obliteration, detachment of the superstructure of the stapes, crural fracture, and profuse bleeding of the thickened lining of the tympanic cavity occasioned by maneuvers within the middle ear (Table 3, Figure 1). Less commonly, there was immobilization of the first and second

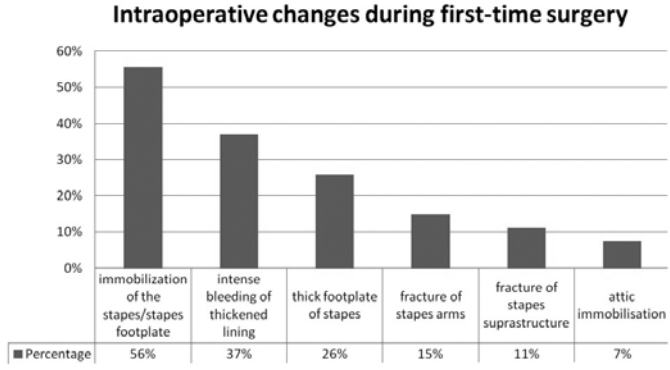

Figure 1. Analysis of intraoperative changes at first surgery among patients with osteogenesis imperfecta.

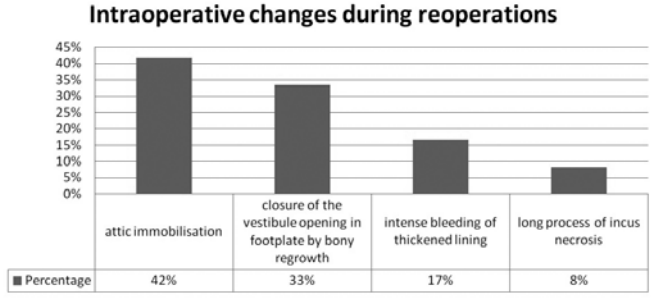

Figure 2. Analysis of intraoperative changes during reoperations among patients with osteogenesis imperfecta.

Table 2. Summary of phenotypic traits of patients with osteogenesis imperfecta

Initials	Blue Sclerae	Number of Bone Fractures	Excessive Laxity of Joints	Lax Skin	Dentinogenesis	Height (cm)	Manner of Move-ment	OI Type (according to Sillence)
OI 1	+	16	–	–	–	170	unassisted	I
OI 2	+	13	–	–	+	165	unassisted	I
OI 3	+	30	–	–	+	150	unassisted	III
OI 4	+	15	–	–	–	178	unassisted	I
OI 5	+	40	–	–	+	147	unassisted	I
OI 6	+	41	–	–	–	151	unassisted	I/IV
OI 7	+	60	+	–	–	140	using a walker	III
OI 8	+	20	+	+	–	161	unassisted	I
OI 9	+	10	+	+	–	160	unassisted	I
OI 10	+	10	+	+	+	170	unassisted	I
OI 11	+	120	+	+	+	102	in a wheelchair	III
OI 12	+	6	+	+	+	164	unassisted	I

OI: osteogenesis imperfecta

Table 3. Summary of types of surgical procedures and intraoperative changes observed during surgeries

No of Patient	Age at First Surgery	OI Type (according to Sillence)	Types of Ear Surgeries and Description of Intraoperative Changes
OI 1	17	I	– stapedotomy of the left ear 2001*
			– stapedotomy with myringo-ossiculoplasty of the left ear 2007 (incus luxation, immobilized malleus, immobilized stapes footplate)
			– stapedotomy of the right ear 2009 (footplate immobilization, crura detached from the footplate)
			– revision remyringo-occisuloplasty of the left ear 2009 (perforation observed in posterior quadrants, correct attachment of the prosthesis in the window, intraoperative bleeding)
OI 2	14	I	– exploratory tympanotomy of the left ear accompanied by removal of the loosely lying superstructure of the stapes 2003 (profuse bleeding)—stage I
			– stapedotomy of the left ear 2003—stage II
			– stapedotomy of the right ear 2004 (stapes immobilization, severe bleeding)
			– restapedotomy of the right ear 2008 (displacement of the prosthesis from the opening in the vestibule, opening covered with osseous tissue)
			– restapedotomy of the right ear 2011 (prosthesis displaced from the opening covered with osseous tissue, loop displacement of the long process)
			– restapedotomy of the right ear 2014 (prosthesis outside the incus, displaced from the oval window covered with osseous tissue, partial necrosis of the long process)
OI 3	32	III	– exploratory tympanotomy of the left ear 2001*
			– myringotomy of the left ear 2002*
			– stapedotomy with ossiculoplasty of the right ear 2008 (immobilized incus and stapes, most probably as a result of early fracture and bone union, exposed facial nerve overlying the oval window, profuse bleeding from the lining)
			– attico-antro-mastoidectomy with the removal of changes and reossiculoplasty 2008 (immobilized incus)
			– restapedotomy with atticotomy and posterior tympanotomy of the right ear 2009 (immobilization of prosthesis by high level of adhesions, correctly placed in the vestibule, immobilized incus, stiffened connection of the short process of the incus and its body with the lateral semicircular canal (callus formation, exposed facial nerve, severe bleeding)

Table 3. Summary of types of surgical procedures and intraoperative changes observed during surgeries (continued)

No of Patient	Age at First Surgery	OI Type (according to Sillence)	Types of Ear Surgeries and Description of Intraoperative Changes
			– revision surgery after stapedotomy of the right ear 2010 (prosthesis among multiple adhesions, incus immobilized in the attic)
			– revision surgery after stapedotomy of the right ear 2012 (multiple adhesions around the prosthesis, incus immobilization— bone union between the body of the incus and lateral wall of the attic)
OI 4	25	I	– stapedotomy of the left ear 2009 (immobilized stapes, enlarged lining of the tympanic cavity)
			– stapedotomy of the right ear 2011 (immobilized stapes, profuse bleeding from the tissues of the auditory canal and the oval window niche)
OI 5	61	I	– stapedotomy of the right ear 2009 (immobilized stapes)
			– stapedotomy of the left ear 2010 (immobilized stapes, thick footplate)
OI 6	63	I/IV	– stapedotomy of the right ear 2011 (immobilized stapes, severe bleeding)
			– stapedotomy of the left ear 2013 (immobilized stapes, persistent bleeding)
OI 7	32	III	– stapedotomy of the left ear 2007 (immobilized stapes)
OI 8	30	I	– stapedotomy of the right ear 2013 (no trace of typical footplate, the entire niche filled with thickened bone, footplate tunnel 3 mm thick)
			– stapedotomy of the left ear 2014 (niche of the oval window covered by thick solid bone, footplate canal length of approx. 3 mm)
OI 9	17	I	– stapedotomy of the right ear 2015 (footplate of the stapes with a thickness of approx. 2 mm, bony overhang in the area of the stapedial footplate)
			– stapedotomy of the left ear 2015 (thick footplate of the stapes, profuse bleeding from the wall of the external auditory canal)
OI 10	49	I	– stapedotomy of the right ear 2016 (immobilized stapes)
OI 11	37	III	– ossiculoplasty of the right ear 2013 (fractures or bony growths on the postero-superior wall of the external auditory canal, bone union between the lateral wall of the attic and the long process of the incus and neck of the malleus, first and second ossicle were mobilized)
			– reossiculoplasty of the right ear 2014 (bone deposits between the long process of the incus and the lateral wall of the attic, immobilization of the malleus and incus, mobile stapes)
OI 12	16	I	– platinectomy of the left ear 2004*
			– stapedotomy of the right ear 2006*
			– partial posterior platinectomy of the right ear 2007*
			– restapedotomy of the right ear 2017 (Teflon prosthesis outside the opening of the vestibule, opening covered with osseous tissue, loop displaced from the long process, extremely narrow and fissured niche of the oval window covered with rigid tissue, immobilized malleus, incus luxation in the incudomalleolar joint, profuse bleeding from the promontory and niche of the oval window)
OI 13	23	/-/	– stapedotomy of the right ear 2006 (fracture of the posterior and anterior crus of the stapes)
OI 14	27	/-/	– stapedotomy and ossiculoplasty of the right ear 2006 (detached superstructure of the stapes from the footplate, excessive mobility of the incus compared to that of malleus)
OI 15	20	/-/	– stapedotomy with myringoplasty of the left ear 2005 (disconnect between the superstructure of the stapes and the footplate)
			– stapedotomy of the right ear 2006 (disconnect between the superstructure of the stapes and the footplate, mobile footplate of the stapes)
OI 16	22	/-/	– explorative tympanotomy of the right ear with removal of the superstructure of the stapes 2003 (immobilized and abnormally developed stapes, profuse intraoperative bleeding) – stage I
			– stapedotomy of the right ear 2003—stage II of the procedure
			– ossiculoplasty of the left ear 2004 (immobilized stapes, part of the footplate became mobile while drilling, severe bleeding)

Table 3. Summary of types of surgical procedures and intraoperative changes observed during surgeries (continued)

OI 17	56	/-/	–	stapedotomy of the right ear 2006 (immobilized stapes, bleeding in the oval window niche)
			–	stapedotomy of the left ear 2006 (immobilized stapes, thick and fragile footplate, partly broken while drilling)
OI 18	45	/-/	–	stapedotomy of the right ear 2007 (immobilized stapes)
			–	stapedotomy of the left ear 2009 (superstructure of the stapes displaced with respect to the long process of the incus, extremely thick stapes footplate)
			–	restapedotomy of the left ear 2015 (opening in the vestibule covered with osseous tissue, slight luxation of the incus, loop of the previously applied prosthesis displaced from the long process)

* surgery performed at another health care center
/-/ lack of information, due to absence at scheduled control
OI: osteogenesis imperfecta

ossicles (fixation in the epitympanum), bony callus covering the body of the incus and the lateral semi-circular canal, and exposure of the tympanic segment of the facial nerve overlying the stapes footplate. Occasionally, all three ossicles were immobilized. From time to time, severe intraoperative bleeding occurred, which prevented safe drilling of the footplate and meant that surgery needed to be done as two separate procedures. When restapedotomy was done, it was seen that the vestibule opening was covered with the osseous tissue, so that displacement of the prosthesis was likely to recur (Figure 2). Similarly, in the case of reossiculoplasty and immobilization in the attic, there was a risk of recurrent fixation and formation of bone deposits (Table 3).

It was also observed in patients OI 3 and OI 11 with OI III type according to Silence that a high number of bone fractures (30 in OI 3 and 120 in OI 11) seem to be connected with a high degree of malformations within the middle ear, which impacts poor audiological results and increases the necessity of reoperations.

DISCUSSION

The intraoperative changes found in the subjects of this study were consistent with those found in the literature [2-6]. Moreover, in this paper, we document changes seen in revision surgeries, which are rarely reported, since the literature usually focuses on first-time surgical procedures [2-12]. Swinnen et al. [3] described two cases of patients who underwent revision surgeries in the form of malleovestibulopexy. One of the patients needed two revision surgeries, as the first procedure revealed necrosis of the long process of the incus, and the second showed fracture of the handle of the malleus. Also, van der Rijt and Cremers [5] reported fractures of the neck of the malleus found during revision surgeries. In one patient, necrosis of the long process of the incus and multiple adhesions in the niche of the oval window were revealed, which had been suggested by profuse bleeding observed during the previous procedure. Vincent et al. [12] described two cases of revision surgeries that involved covering of the opening in the footplate of the stapes and displacement of the prosthesis. In most of the cases, the hearing improvements obtained from revision surgeries were less significant than those from first-time surgeries, a result that was also found by Swinnen et al. [3], Shea et al. [7], and Vincent et al. [12].

The present study showed that in long-term observations of this group of patients, it was sometimes necessary to perform revision surgery due to constant bone regrowth-covering of the opening in the vestibule and recurrent immobilization of the ossicles in the attic. It was also observed that the greater the number of changes in the patient's phenotype (i.e., the greater the number of bone fractures, more advanced bone deformities), the more changed were the anatomical conditions in the middle ear. Young age at the time of the first surgical procedure and elevated phenotypic traits of OI may be predictors of an increased risk of revision surgery in the future. Immobilization of all three ossicles and revision surgery secondary to a procedure carried out at a health care center with limited experience in this field both appear to be unfavorable predictors so far as obtaining long-lasting hearing effects and avoiding the need for revision surgery are concerned. Severe bleeding indicates that a staged stapedotomy may be necessary.

CONCLUSION

Stapedotomy and ossiculoplasty are the treatments of choice for conductive or mixed hearing loss in patients with OI. The most common pathology within the stapes may be effectively treated by stapedotomy. The greater changes induced systemically by osteogenesis imperfecta, the greater the risk of significant malformations in the middle ear. Patients with OI are at an increased risk of needing revision surgery and suffering intraoperative complications such as bleeding, which hinders safe completion of the procedure. Long-term observation of hearing is indispensable, especially in young patients, since bone regrowth may lead to hearing impairment and require revision surgery.

Ethics Committee Approval: This publication is based on approval of Bioethics Committee of the Institute of Physiology and Pathology of Hearing IFPS: KB/14/2016. This approval is consistent with The Code of Ethics of the World Medical Association.

Informed Consent: The informed consents were not necessary due to the retrospective nature of this study.

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