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REVIEW OF TEMPORAL BONE MALIGNANCY WITH CRITICAL APPRAISAL OF LONG-TERM OUTCOMES FOR SURGICAL MANAGEMENT: SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Purpose: The purpose of the study is to investigate the trends in long term outcomes for surgical treatment of temporal bone malignancy and generate guidelines for future benchmark reference, in order to establish a treatment pathway for critical decision making, supported by cumulative evidence gathered over decades of research. Apart from this, the study will aim to answer four key questions in relation to temporal bone malignancy: (1) Has survival for temporal bone malignancy improved over the last few decades (2) Is Total temporal bone resection ever indicated ? (3) How does prognosis change when structures such as the dura mater, brain and internal carotid artery become involved ? What is the feasibility of surgery in these instances ? (4) What is the role of postoperative radiation therapy ? **Materials and Methods:** A systematic review was conducted to study the long term outcomes of surgical management of temporal bone malignancy. 736 articles had been published till October 2018, which included retrospective studies, prospective studies, SEER Database surveys, Multicenter studies and smaller descriptive studies. References of the selected studies were further searched for relevant articles. Apart from this, a search was conducted over Google Scholar to obtain related articles. Subsequently, a meta-analysis was completed to extrapolate the cumulative survival, hazard rate, survival probability and event rate for surgical management of temporal bone malignancy. Following this, regression analysis was conducted to study the outcomes of primary surgery +/- adjuvant radiotherapy as a treatment protocol for temporal bone malignancy. **Results:** The long term outcomes for surgical management of temporal bone malignancy have improved over the last few decades. Also, outcomes for surgical management of advanced stage disease show a favourable trend. Further clinical trials and multicentre studies should be carried out to strengthen the results for this separate clinical cohort. Primary surgery +/- adjuvant radiotherapy has commendable long term clinical outcomes in the contemporary skull base era. **Conclusion:** Long term outcomes for surgical management of temporal bone malignancy show slow but persistent improvements resulting from the parallel consistent development of skull base surgical techniques.

KEYWORDS: Temporal bone carcinoma; outcomes; survival; surgical management; primary surgery; temporal bone malignancy; carcinoma external auditory canal; middle ear cancer; treatment temporal bone carcinoma; long term outcomes; survival outcomes; lateral skull base malignancy.

INTRODUCTION

As is truth from lie and facts from fallacy, it is hard to distinguish the uncommon from the not so uncommon. If to speak of temporal bone malignancies, the incidence reported may be extremely low, only until one encounters an obvious presentation, when least expecting. As they say “chance favours the prepared mind”, the surgeon behold watchful, lest the diagnosis would be missed, only to end as the most ominous consequences for an innocent patient. The incidence reported for temporal bone malignancies is between 1 and 6 per million, such that cancers of external auditory canal and temporal bone comprise less than 0.2% of all head and neck cancers.[1-3] The demographics are well reported with a typical male to female ratio of 2:1 and up to 20% cases affecting the pediatric age group. The overall age is in the range of 40-75 years.[4-8] 60-80% of the malignancies are identified as squamous cell carcinomas, while 20% are adenoid cystic carcinomas or adenocarcinomas. Primary basal cell carcinomas of temporal bone occur seldom, while melanomas are even more rare.[4] Majority of tumours in adult age group are squamous cell carcinomas, while most in pediatric age group are rhabdomyosarcomas, thus exhibiting a bimodal distribution of tumour incidence.

Baldo et al,[10] presented their results on primary tumours of the external auditory canal (EAC) while Gurgel et al,[11] published one of the most extensive review on middle ear carcinomas. Though, Stell et al.[12] reported no difference between the outcomes of tumours originating in EAC and middle ear, it is well known from the distinguishably recognized work of Spector et al,[13] that the more medial and deep is the invasion of the tumour, the more disappointing is the prognosis, such that all efforts towards treatment would be futile unless one resolves to more radical surgical management which may be accompanied by adjuvant therapy. Kawana et al.[14] have reported clear differences in outcomes for the two sites. To give an overview of middle ear carcinomas, it is pertinent to elaborate the study by Gurgel et al (2004) who presented an analysis of the SEER Database to bring out patterns of incidence, treatment and survival of primary middle ear carcinomas over a period extending from 1973 to 2004. The 5-year observed survival rate for 215 patients was 36.4%. This large sample size included 62.8% squamous cell carcinomas, 18.2% adenocarcinomas, 13% were other carcinomas, while 6% were noncarcinomas. 31.2% patients had been treated by surgery, 16.3% by radiation, 38.6% by surgery with postoperative radiotherapy and 8.4% had no treatment. The 5-year survival rates for these four groups were 69.2%, 14.6%, 26.4% and 0% respectively. A similar study has been presented by Shen et al.[15] in 2014. The 5-year overall and cause-specific survival rates for 247 patients with middle ear carcinoma were 47.4% and 58% respectively.

Diagnosis

"Thou search for truth as a seeker, true colours will bleed". Such is the diagnosis for temporal bone malignancies, many a times hidden to the untrained mind more than the untrained eye. It is but for the veil of usual symptomatology that conceals the hidden malignancy, such that repeated biopsies would be required in most of the cases. Directions are less and misdirection more, the surgeon has be persistent in his effort to uncover the true pathology. Often, the symptoms would merely be reported as otorrhoea and pruritis. Though less commonly, there may be an obvious classical presentation consisting of bloody discharge with tinnitus, facial paralysis, severe pain, vertigo or sensorineural hearing loss. An unforgiving deep temporal pain usually signifies bony or dural invasion. As for the time of onset, the patient may report a duration of symptoms from 4 months to 4 years.[7] There could be a history of previous mastoid surgery, such that the diagnosis awaits several biopsy attempts, for the histopathologic assessment is further complicated by tissue necrosis, secondary infection and haemorrhage. The finding of trismus should alert the clinician towards possibility of infratemporal fossa or involvement of temporomandibular joint, due to invasion of medial or lateral pterygoid muscles.

Preoperative imaging for accurate mapping of boundaries for resection is indispensable. While CT scans can reveal areas of bone erosion, MRI is required to elaborate spread of tumour along neural pathways, vascular channels, intracranial extension and involvement of extra-temporal soft tissues. The experienced observer would keep in mind the pathways of invasion for temporal bone malignancy while evaluating the findings on imaging. In this regard, it would be pertinent to mention the landmark publication by Leonetti,[16] et al who described the following patterns of tumour spread:

1. Superior erosion through tegmen tympani into middle cranial fossa
2. Anterior extension into glenoid fossa and infratemporal space
3. Inferior growth through the hypotympanum and jugular foramen
4. Posterior involvement of mastoid air cells and
5. Medial involvement of middle ear and carotid canal

As every imaging modality suffers from its own limitations, it is difficult to predict the anterior soft tissue extent of tumour on CT imaging.[8,17] It is well known that the tumour can extend anteriorly through the cartilaginous fissures of Santorini and Huschke's foramen preceding any identifiable erosion of bony canal.[18] There is a tendency towards underestimation of disease in infratemporal fossa, mastoid cavity and carotid canal. Of utmost importance is the extension of tumour medially into middle ear cavity, with resultant direct implication towards the type of surgical resection required. The tumour may erode inner ear structures, infiltrating the labyrinth through lateral semicircular canal, round window or oval window. Such infiltration may show further proximal extension along vestibular or cochlear nerves into internal acoustic canal. Although the resistant cortical bone of inner ear, in particular the otic capsule, limits the amount of gross bone destruction, more aggressive tumours would eventually reach the cochlea. Extension posteriorly into mastoid antrum, through the aditus, is more readily gained, while further posterior extension leads to involvement of sigmoid sinus and posterior cranial fossa. A tumour extending superiorly into middle cranial fossa will test the judgement of the examiner, who must distinguish temporal lobe oedema from actual cerebral parenchymal infiltration. In case of advanced tumours with possible involvement of petrous internal carotid artery and sigmoid sinus, vascular signal void and flow enhancement can be distinguished on post-contrast MRI.[19] Erosions less than 2 mm deep in bony walls of EAC, usually cannot be detected on preoperative imaging.[20]

More recently, Razek,[21] (2018) presented a study with the most intriguing results that could mean a paradigm shift in the imaging and diagnosis of temporal bone malignancy. The authors revealed the utility of diffusion-weighted MRI (DW-MRI) in a retrospective analysis of

43 cases. The outcomes were correlated in terms of apparent diffusion coefficient (ADC) value, which not only allows differentiation of malignancy from benign lesions, but also distinguishes well and moderately differentiated malignancy versus poor and undifferentiated malignancy, apart from stratifying stage I and II disease versus stage III and IV disease.

Staging

If one were to carefully review the early literature on treatment of temporal bone malignancies, it appears obvious that the various case series reporting meaningful data are not apt to comparison due to a lack of uniform staging system. It was late until 1990, when Arriaga et al[5] proposed the Pittsburgh Staging System (Table 1). This was the first staging system to receive an overwhelming acceptance throughout different continents, as a consequence to which, Moody et al,[3] presented their modification to Pittsburgh Staging System, according to which lesions clinically presenting as facial nerve paralysis were classified as T4. More recently, Mazonni et al,[22] proposed subcategories for T4, in the light of which, T4b cases have worst prognosis as compared to T4a due to extension of tumour medially, inferiorly and posteriorly into temporal bone and skull base (Table 2).

History

In the words of the Sensei, honourable Miyamoto Musashi – "Start learning from zero and there is no end to the number of techniques that will emerge".

Though surgical treatment for malignancies of the temporal bone and external ear canal had been practiced more than a century ago, it was not until 1951 when Campbell et al,[23] first gave an accurate description of "Total" temporal bone resection. Before this period, temporal bone malignancies had been mostly managed with radical mastoidectomy. Thereafter, many new techniques appeared in the English language literature over the coming decade. Parsons and Lewis,[24] in 1954, described "Subtotal" resection of temporal bone. A few years later, Conley and Novak,[25] presented their technique of "Lateral" temporal bone resection in 1960. Due to the comparatively little radicality of this procedure, it was readily accepted across many continents, thence would appear modifications to this procedure, suitably adapted to the various extents of involvement by temporal bone malignancy. In the meanwhile, Lewis.[26] presented his experience with a large number of 150 cases in 1960. Over the years to follow, the terminologies "Total", "Subtotal" and "Lateral" temporal bone resections gained wide acceptance and eventually came to be recognised as standardized techniques in various textbooks, thus representing an hierarchy of less extensive to more radical procedures but each matching to its own suitable indications. "Sleeve resection" involves removal of skin of the external auditory canal. "Lateral temporal bone resection" (LTBR) includes enbloc removal of bony and cartilaginous external auditory canal along with tympanic membrane, malleus and incus. It may be extended to include the parotid, temporomandibular joint, zygoma and infratemporal fossa. "Subtotal temporal bone resection" (STBR) entails removal of structures sacrificed in LTBR along with piecemeal or enbloc resection of tumor in the middle ear and mastoid, otic capsule, medial wall of middle ear, and mastoid. Dependent on spread, it may be extended to encompass the facial nerve, dura, contents of infratemporal fossa and sigmoid sinus. "Total temporal bone resection" (TTBR) involves resection of structures included in STBR, along with petrous apex. Again, depending on the invasion patterns, it may include resection of tumour along jugular foramen, carotid canal, dura, other cranial nerves and lateral temporal lobe.

In a classic paper by the famous Jesus Medina,[27] he described four subcategories of Lateral temporal bone resection, when he reported his retrospective analysis of 18 consecutive patients : Type I – consists of removal of tympanic bone and the external auditory canal (EAC) lateral to tympanic membrane. Type II resection would consist of removing the entire tympanic bone, the tympanic membrane, the incus and the malleus, preserving the facial nerve and inner ear. Type III resections consisted of resecting the structures in Type II but also the distal facial nerve and fallopian canal, the mastoid tip, styloid process and stylomastoid foramen. Type IV resection rather was completely different from Type III, such that it involved removal of only the mastoid tip and inferior portion of tympanic bone. This however, does not conclude the discussion here. As various authors presented their experiences, further techniques appeared. More recently, Ghavami et al,[28] (2017) have proposed a modification of the standard LTBR, whereby the tympanic membrane and ossicles are spared, in order to preserve hearing. However, the mean follow-up time reported was only 29.2 months and 5 year results are awaited.

Spector et al,[13] have intriguingly described the evolutionary trends in the management of temporal bone carcinomas, comparing survival tendencies from two different eras in time. A large sample size of 51 patients was divided into two groups – 17 patients who were treated over a 20 year period from 1960 to 1980, compared to 34 patients who were studied from 1980 to 1989. These subjects were further stratified into four groups, based on the initial tumour presentation and location - external auditory canal, superficial invasion, deep invasion and tumors beyond the temporal bone. The first group was treated with various combinations of surgery and radiotherapy, such that the 5-year cure rates were 70%, 70%, 50% and 9% respectively. The second group was studied for outcomes of formal standardized surgical techniques, viz. external canal tumors were managed by sleeve resection of the internal auditory canal along with tympanic membrane, superficial invasion by superficial temporal bone resection, deep

tumors by radical temporal bone resection and those beyond the temporal bone by an infratemporal fossa approach. Over a follow-up period of 36.6 months, the cure rates for the four groups were 100%, 100%, 70% and 65%, respectively.

Purpose

The purpose of the study is to investigate the trends in long term outcomes for surgical treatment of temporal bone malignancy and generate guidelines for future benchmark reference, in order to establish a treatment pathway for critical decision making, supported by cumulative evidence gathered over decades of research. Apart from this, the study will aim to answer four key questions in relation to temporal bone malignancy: (1) Has survival for temporal bone malignancy improved over the last few decades (2) Is Total temporal bone resection ever indicated? (3) How does prognosis change when structures such as the dura mater, brain and internal carotid artery become involved? What is the feasibility of surgery in these instances? (4) What is the role of postoperative radiation therapy?

MATERIALS AND METHODS

An electronic search was conducted using the terms “temporal bone”, “outcomes”, “surgical procedures” and “neoplasms” in combination with the following search strategy : Search block Temporal bone -(("Temporal Bone"[Mesh] OR temporal bone*[tiab] OR "Ear Canal"[Mesh] OR external ear canal*[tiab] OR external auditory canal*[tiab] OR external acoustic canal*[tiab] OR external acoustic meatus[tiab] OR Mastoid[tiab] OR Petrous Bone*[tiab] OR petrous pyramid*[tiab] OR os temporal*[tiab] OR processus zygomaticus[tiab])); Search block Outcomes -("Outcome Assessment (Health Care)"[Mesh] OR "Treatment Outcome"[Mesh] OR long term*[tiab]); Search block Surgical procedures - "Surgical Procedures, Operative"[Mesh] OR "surgery" [Subheading] OR surgery*[tiab] OR surgical*[tiab] OR operative procedure*[tiab] OR resection*[tiab] and Search block Neoplasms - "Neoplasms"[Mesh] OR neoplasm*[tiab] OR carcinoma*[tiab] OR cancer*[tiab] OR malignancy*[tiab] OR tumor*[tiab] OR tumour*[tiab] OR neoplasia*[tiab]. Clinical studies were retrieved from the electronic databases of PubMed, EMBASE, SCOPUS and Cochrane Library. 736 articles had been published till November 2018, which included retrospective studies, prospective studies, SEER Database surveys, multicenter studies and smaller descriptive studies. References of the selected studies were further searched for relevant articles. Apart from this, a search was conducted over Google Scholar to obtain related articles.

Cumulative Hazard Rate was obtained using meta-analytic methodology. 67 studies were included into this meta-analysis, so as to obtain a large sample size, in order to bring out trends in improvement of survival time over the past three decades. Studies incorporating results of primary radiation or chemoradiation were excluded. Median survival rate was calculated for overall survival from a group of 45 studies which included enough information on various parameters, excluding studies with primary radiation or chemoradiation as one of the treatment arms. A meta-analysis of proportions was completed based on these 45 studies, through inverse-variance fixed effects model (recommended for time-to-event data) followed by random effects DerSimonian-Laird model (accounts for heterogeneity) generating an overall event rate and forest plots were constructed. Subsequently, cumulative meta-analysis was completed for both models. Overall survival probability was calculated through the meta-analysis, to provide 5-year survival estimates as a reflection of temporal trends in survival outcomes, in relation to primary surgery as the major treatment modality. In order to identify and remove heterogeneity, strict selection criteria were employed as per the recommendations mentioned by the working committee on PRISMA guidelines, such that only the studies on primary surgery as the main treatment modality, with or without adjuvant therapy, were included in the meta-analysis.

In order to explore the survival outcomes for primary surgery as a treatment protocol for temporal bone malignancy, Cox regression was carried out over a dataset of 45 studies which contained adequate information in relation to primary surgery for subgroup analysis, so as to bring out the influence of primary surgery as a covariate on the overall survival time for temporal bone malignancy. As a prerequisite, it was proved through linear regression that there was definite association between the survival time and this covariate, followed by binary logistic regression to strengthen the results. Subsequently bootstrapping was done to establish the predictive ability of the treatment model. In all of the above mentioned calculations, Confidence level was 95%.

Legends for figures

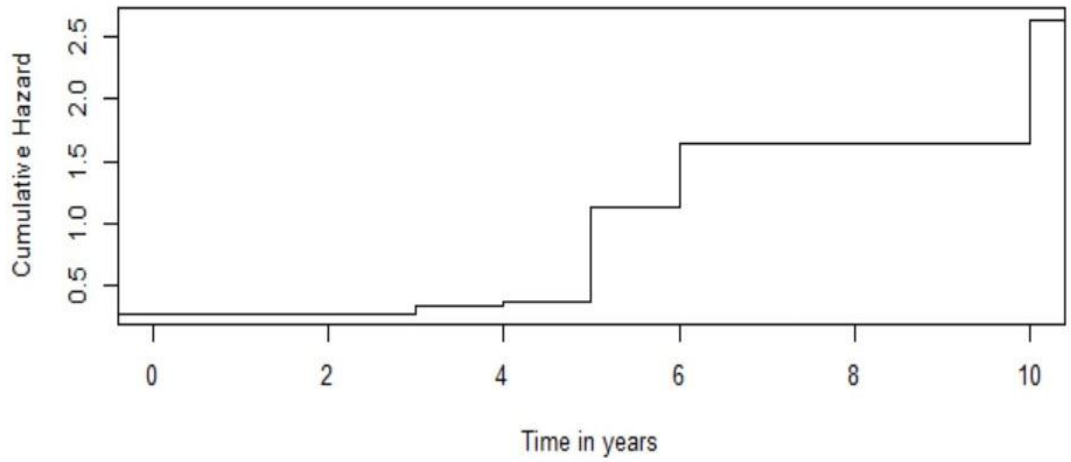

Fig. 1: Curve representing cumulative hazard rate.

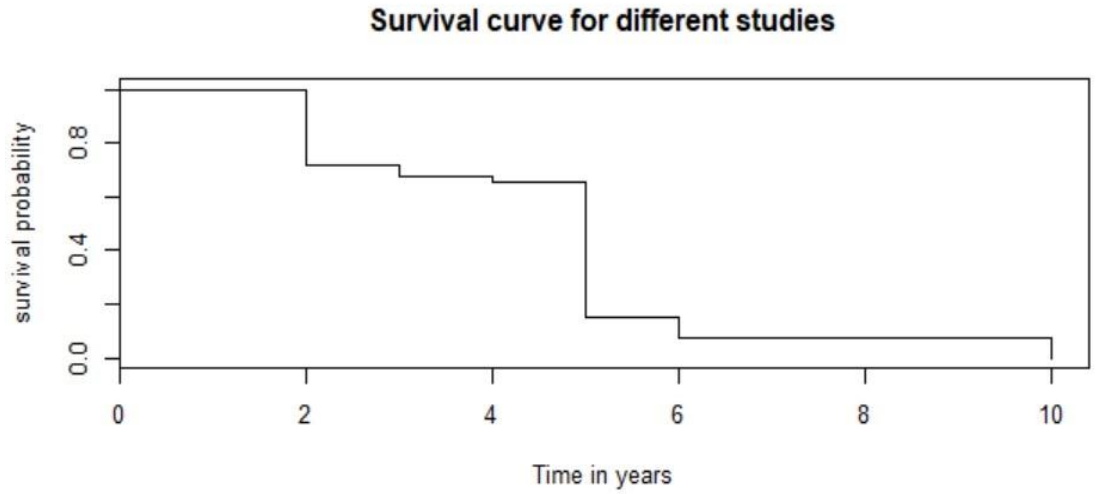

Fig. 2: Curve representing survival probability.

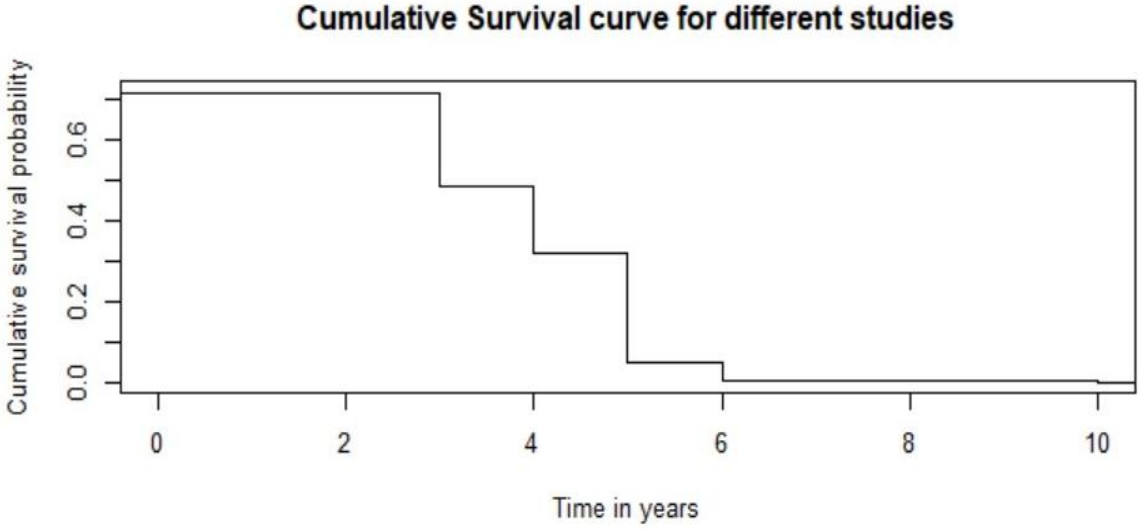

Fig. 3: Curve representing cumulative survival probability.

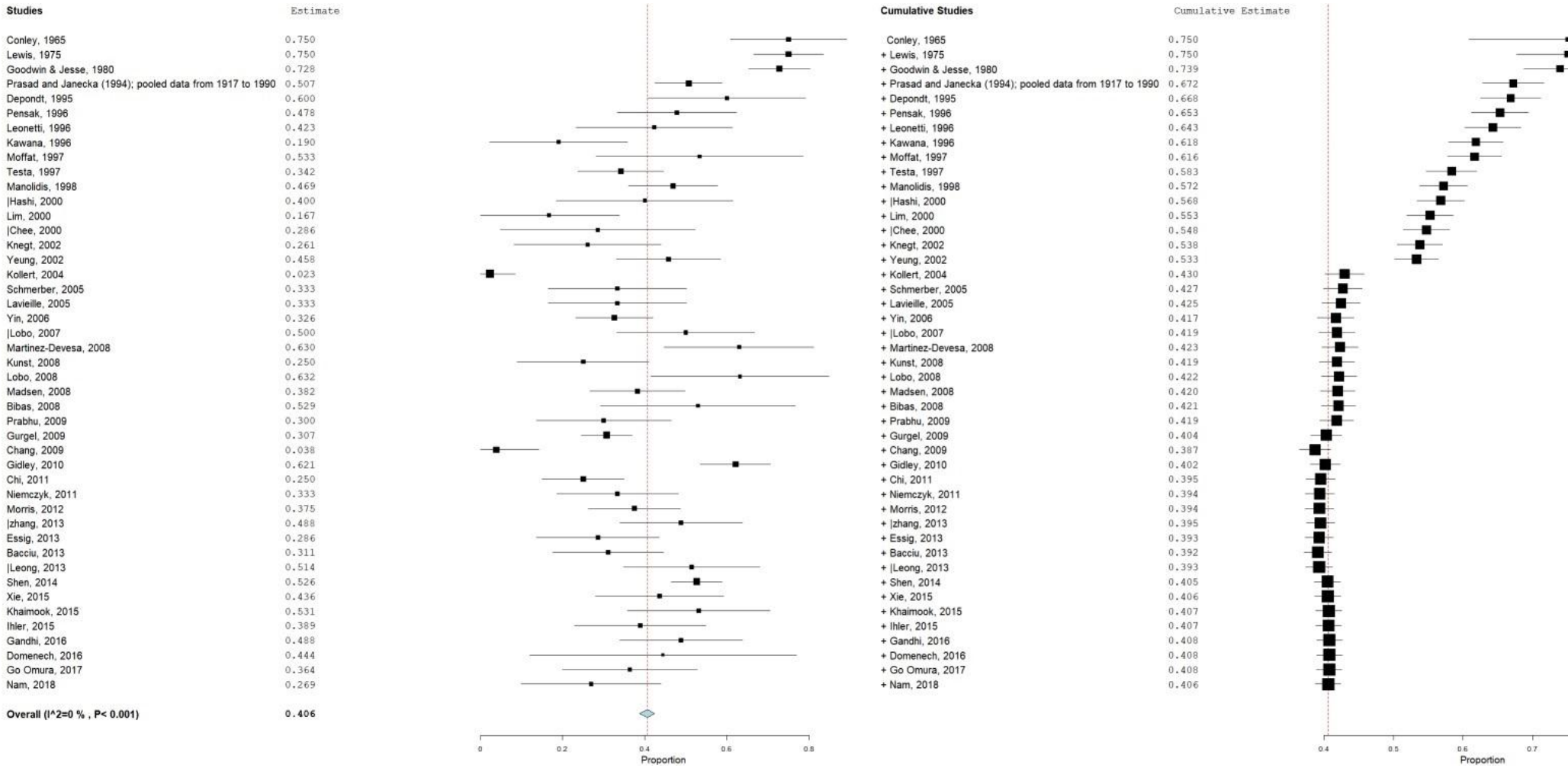

Fig. 4: Forest plot for fixed effects inverse-variance model.

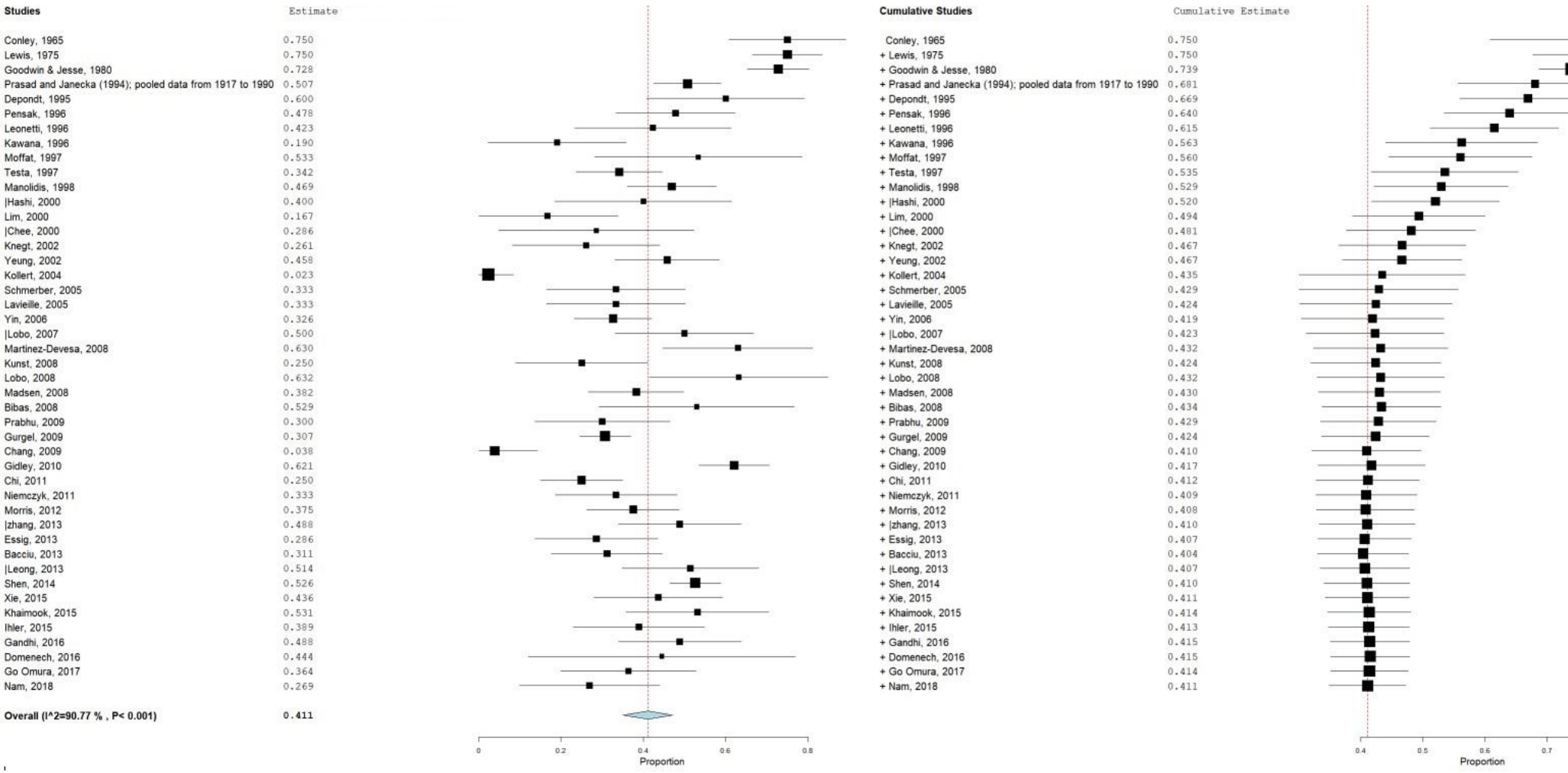

Fig. 5: Forest plot for random effects DerSimonian Laird model.

Table 1: Pittsburgh Staging System for Temporal Bone Carcinoma.

T1	Tumour limited to external auditory canal without bony erosion or evidence of soft tissue extension
T2	Tumour with limited erosion of external auditory canal (not full thickness) or radiographic finding consistent with limited soft tissue involvement
T3	Tumour eroding the osseous external auditory canal (full thickness) with limited (< 0.5 cm) soft tissue involvement, or tumour involving middle ear and / or mastoid, or patients presenting with facial paralysis
T4	Tumour eroding the cochlea, petrous apex, medial wall of the middle ear, carotid canal, jugular foramen or dura, or with extensive (> 0.5 cm) soft tissue involvement

Table 2: Pittsburgh Staging System for Temporal Bone Carcinoma as modified by Mazzoni et al.

Stage	Table 2: Site and Subsites
T1	Tumour in skin with no bone involvement
T2	Tumour in skin with bone / cartilage involvement, but not full thickness
T3a	Tumour extending < 5 mm from cartilage to periauricular soft tissues, or Tumour strictly limited to the anterior bone wall and growing < 5 mm into the parotid space
T3b	Same as for T3a, but extending > 5 mm
T4a	Tumour growing into the mastoid, without facial nerve palsy
T4b	Tumour growing into the mastoid with facial palsy, or into the infratemporal space, or the medial wall of the tympanum, or labyrinth, or petrous bone (jugular foramen, internal carotid canal, petrous apex)

Table 3: Survival Outcomes.

Author	n (no.of subjects)	Follow-up and type of survival data	Survival in Percentage				
			T1	T2	T3	T4	Overall
Conley, 1965	36						25
Lewis, 1975	100						25
Goodwin & Jesse, 1980	136					29	27
Arriaga, 1989	35	2 years	100	100	50	15	
Kinney, 1989	30	2.5 years	92		72	45	
Liu, 1993	29	6.1 years					5 y DSS 50
Austin, 1994	22	3 years	S1 60	S2 100	S3 50	S4 50	
Prasad and Janecka (1994); pooled data from 1917 to 1990	144	Cumulative					49
Depondt, 1995	25	2 years					2 y OS for SCC 38
Pensak, 1996	46	Mean 6.5 years					51
Leonetti, 1996	26						58
Kawana, 1996	21	5 years					EAC: 77.8 Middle ear: 40
Moffat, 1997	15						47
Testa, 1997	79	5 years					Surgery 65 Radiotherapy 29 Surgery + Radiotherapy: 63
Manolidis, 1998	81	5 year RFS					53.1%
Pfreunder, 1999	27	5 years	86		50	41	
Moody, 2000	32	2 years	100	80	50	7	
Hashi, 2000	20	5 years					59
Lim, 2000	18						80
Chee, 2000	14	2 years DFS					69
Schwager, 2001	30	5 years	89	89	S3 67	S4 39	
Gillespie, 2001	15	2 years	100	100	50	15	
Nyrop, 2002	20	2 years	Cure rates S1 91	S2 100	S3 0	S4 0	
Knegt, 2002	23	5 years 10 years					5 y OS 74 10 y OS 60

Tiwari, 2002	25	5 years					5 y DFS 42
Yeung, 2002	59	5 years DSS	90	45	40	19	54
Kollert, 2004	21	5 years					Primary: 100 Salvage: 33
Schmerber, 2005	30	5 years	82	82	67	17	Overall complete remission: Primary surgery 65
Lavieille, 2005	30	2 years	82		67	32	Overall complete remission: Primary surgery 64.7
Moffat, 2005	39	2 years			50	38	Overall DFS 43.2
Yin, 2006	95	5 years	S1 100	S2 100	S3 67.2	S4 29	5 y OS 66.8
Lobo, 2007	34	5 years DFS	87	87	21	21	49
Martinez-Devesa, 2008	27	3 years & 5 years	S1 100	S2 >24 mos	S3 16 mos	S4 9 mos	3 year OS 38
Kawahara, 2008	17	5 years					DSS 60.1 RFS 67.5
Kunst, 2008	28	10 years	85	85	46	46	2 y OS 75 10 y OS 64
Lobo, 2008	19	5 years		S2 100	S3 25	S4 16	5 y OS 37 5 y DFS 37
Madsen, 2008	68	5 years					Surgery Group OS 60.6 DSS 75.8
Okada, 2008	18	2 years & 5 years					2 y OS 86 5 y OS 78
Bibas, 2008	17	5 years					OS 47.06 DSS 64.17
Kang, 2009	35	3 years					3 y DSS 80 3 y DFS 63
Prabhu, 2009	30	5 year actuarial probability					Early Stage 70 Advanced Stage 41
Gurgel, 2009	215	5 years	Local Disease: 69.1		Regional Metastasis: 34.2		Surgery group: 69.2 ; Radiotherapy group: 14.6; Surgery + RT: 26.4
Cristalli, 2009	17	2.5 years					OS: 75.6 DFS: 73.3
Chang, 2009	12	4.7 years DFS					Early stage 100 Late Stage 20
Dean, 2010	65	5 years					2 y DFS: 67.6 5 y DFS: 50.2
Gidley, 2010	124	5 years					OS for SCC 38 Early stage 48 Late stage 28
Chi, 2011	72	5 years	100	67	21	14	5 y OS: 75
Niemczyk, 2011	39	2 years					2 y OS 67 Tumours confined to EAC 100
Morris, 2012	72	5 years					5 y OS 62 5 y DSS 70 5 y RFS 46

Zhang, 2013	43	5 years					5 y OS 51.7
Lassig, 2013	30	2 years					2 y DFS 70
Essig, 2013	35	5 years					2 y OS 72 5 y OS 49
Bacciu, 2013	45	5 years					5 y OS 67.6 5 y RFS 68.9
Leong, 2013	35	5 years					5 y OS 48.6
Ugumori, 2013	41	5 years	100	100	20.8	27.5	
Shen, 2014	247	5 years					5 y OS 47.4 5 y Cause specific survival: 58
Li, 2014	12	2 years					DFS of 42.3 for malignancies extending to jugular foramen
Zhen, 2014	16	2 years					2 y DFS 62.5
Mazzoni, 2014	41		50	83.3	75	29.3	
Zanoletti, 2014	41	5 years					DSS: 61
Xie, 2015	39	2 years	S1 100	S2 100		S4 22.3	56.9
Khaimook, 2015	32	2 years	100	100	100	46.2	46.9
Ihler, 2015	36	5 years					R0: 59.4 R1: 56.6
Gandhi, 2016	43	2 years					2 y OS 50.7
Domenech, 2016	9	2.25 years					55
Go Omura, 2017	33	5 years					5 y OS 62 5 y DSS 71
Nam, 2018	26	5 years					5 y OS 70.4 5 y RFS 61.8

Abbreviations : OS - Overall Survival, DFS - Disease Free Survival, RFS - Recurrence Free Survival, S1 - Stage I, S2 - Stage II, S3 - Stage III, S4 - Stage IV, 2 y - 2 years, 3 y - 3 years, 5 y - 5 years, 10 y - 10 years.

Table 4: Studies reporting Total TBR.

Author	n (no. of cases involving Total TBR)
Wu, 1984	22
Arriaga, 1989	6
Austin, 1994	2
Manolidis, 1998	12
Hashi, 2000	5
Moody, 2000	5
Stankovic, 2004	2
Kunst, 2008	3
Lobo, 2008	5

RESULTS

The four questions outlined in the section of purpose of study have been adequately answered in the foregoing discussion. As such, it can be inferred that Total Petrosectomy, i.e. Total temporal bone resection without sacrifice of internal carotid artery, is an acceptable procedure with favourable outcomes, as reflected by the results of numerous new studies. On the other hand, Total temporal bone resection with sacrifice of the internal carotid artery requires more focussed clinical trials at tertiary and quaternary level institutes with facility of BTO and carotid reconstruction. However, since studies on this subject are limited by the low incidence of disease, efforts would have to be shaped in direction of multicenter trials, such that prospective data can be incurred for generating benchmark references. Also, some selected cases with invasion of cavernous sinus and temporal lobe, could be managed by primary surgery followed by postoperative radiotherapy, as per the treatment protocol set by Moffat et al,[56] preferably at centers specialised in skull base surgery, so that results are not degraded by the limitation of facility and expertise. Only then, adequate evidence can be generated to guide further treatment protocols without biased decisions and personal opinions. A treatment strategy cannot be called inferior simply because of the lack of expertise. As far as question of quality of life is concerned, critics must learn to choose between death

and life, rather than choosing between death and quality of life. So far so, that quality of life would turn into quality of death, if patient is denied the chance of possible surgical treatment, by labelling it as inoperable. As the surgical community knows well, inoperability is a subjective judgement, limited by the experience and expertise of the surgeon. A pertinent reflection of this fact can be seen in the revised UICC staging of cancer, where the words "resectable" and "unresectable" have been replaced by the words "advanced" and "very advanced", respectively.

As far as the statistical results are concerned, a cumulative hazard rate was calculated from a large pool of 67 studies, using meta-analytic methodology. For the purpose of discussion, it must be emphasized, this meta-analysis is valid as per Glass' original description of the meta-analytic methodology, whereby a cumulative result is generated from a large pool of studies, rather than generating a summary of 10 to 15 studies. At the same time, it justifies Rosenthal's definition of meta-analysis, by creating quantitative inference from a group of studies, which can be correlated with prognostic variables and change in survival trends over time. Also, as per the guidelines for meta-analysis of time-to-event data, the first and foremost outcome should be cumulative hazard rate. This was calculated with the help of specialised professional software R (version 3.5.1, Institute for Statistics and Mathematics, Vienna, Austria; www.r-project.org), designed especially for the purpose of meta-analytic review and recognised throughout the world as a valid statistical tool. The cumulative hazard rate was 0.283 at 2 years and 1.141 at 5 years (Fig. 1). Similarly, survival probability was obtained from these 67 studies (Fig. 2), the value being 0.716 at 2 years and 0.047 at 5 years. Survival probability provides an accurate estimate of success and validity of a treatment protocol for time-to-event data (Fig. 3). It is considered a basic reference for comparing effects of various prognostic variables.

The Median overall survival rate was calculated from 45 studies, the value being 59%, such that the remaining 22 studies had to be censored because of insufficient details, in order to produce an unbiased resultant value, free from the effect of heterogeneity. Also, studies including preoperative radiation or chemoradiation were excluded. This obtained value shows a large improvement over a cumulative survival rate of 49%, as reported by Prasad and Janecka,[36] in 1994, thus underlining the changes in outcomes with the development of skull base surgery as a recognised speciality with transcending applications in field of temporal bone resection. Apart from that, it represents a paradigm shift for primary surgery as a time-tested treatment modality, with regards to temporal bone malignancy, based on evidence gathered over decades of research. The cumulative survival was 0.716 at 2 years and 0.149 at 5 years. For the meta-analysis of proportions, the overall estimate was 0.406 (event rate, with death as event, Fig. 4) with the inverse variance method and 0.411 with the random effects DerSimonian-Laird Model (Fig. 5), obtaining a p value < 0.001 in both instances (Confidence level 95%), thus significant. Further, a subgroup analysis was done for 22 studies, so as to identify trends in outcomes of T1, T2, T3 and T4 tumours separately and the underlying correlations between primary surgery as a treatment protocol and staging of temporal bone malignancy. The median survival outcomes for T1, T2, T3 and T4 subgroups were 91%, 88.94%, 67% and 30.65% respectively. This subgroup analysis reveals the slow but persistent improvement in outcomes for advanced stage T3 and T4 disease, when compared to a rate of 50% and 7%, for T3 and T4 respectively as reported by Moody et al,[3] in 2000. It can be proposed that Total Petrosectomy without sacrifice of internal carotid artery, is a safe and established treatment protocol for advanced stage temporal bone malignancy, with adjuvant postoperative radiotherapy as a symbiotic companion for providing best treatment results in favour of patient as the priority. The debate of internal carotid artery sacrifice has been reopened as a result of publication by Back et al,[104] such that unbiased efforts should be conducted in this direction without unprofessional and derogatory criticism. The procedure which should have been established by 1990's after the initial report by Graham et al,[105] (1984), deserves persistent research and respect of a valid treatment protocol in this skull base era, where much more is possible as compared to 1984.

Both linear regression and binary logistic regression obtained a p value < 0.05, hence significance achieved. The cox regression was based on cox proportional hazards model. The Cox Hazards Ratio was 0.9561 and p value was 0.00086 ($p < 0.05$). The results were thus significant. By inserting these values into standard formula, it can be inferred that the risk of death is 4.39% less if patients are treated through primary surgery. The results of cox regression have proved that primary surgery is a valid treatment protocol for temporal bone malignancy and is associated with prolongation of survival. The mean survival time for primary surgery group was 4.97 years.

DISCUSSION

The outcomes for surgical management of temporal bone carcinoma have transcended into the era of skull base surgery, whereby surgical techniques that evolved over a century of persistence have led to dramatic improvements in results of surgical management (Table 3). This is clearly evident if one compares the results with a century ago, when Newhart et al.[91] presented the first well documented case series in 1917. Research endeavours have helped to identify definite prognostic factors.[73,78,79,83,84,86,89,92-94] which guide stratification of surgical management as per the staging and outcomes data. However, there is no single prognostic factor which can be overemphasized, the outcomes being affected by an underlying interplay of different cause-effect relationships in the light of progressively accumulating

survival data. Though some authors point out the non-homogenous nature of outcomes data, there are now multicenter studies available, which has made all the difference in terms of level of evidence. Also, outcomes are now retrievable for different surgical techniques from a homogenous group of studies which describe results of surgical intervention for specific histopathological types, along with radiologic-pathologic correlations in a large sample size, there being more than 10 studies available for each surgical technique. However, the present manuscript will focus on outcomes of temporal bone malignancy as a whole, in relation to surgical management, analysing a large data set. It would be meaningless to conduct a systematic review including 10 to 20 studies based on specific surgical techniques or particular histopathologic types.

Ever since Newhart et al.[91] described a case series of patients suffering from temporal bone carcinoma in 1917, more than 50 case series have been published in English, Japanese, French, Italian and Spanish languages. Though Newhart merely described the clinical signs and symptoms for this disease, the classic surgical techniques of total, subtotal and lateral temporal bone resection were described much later. As such, any valuable relevant data became available only after the adoption of standardized surgical techniques. The first largest case series was reported by Lewis et al in 1960,[26] who presented results of 150 cases from Memorial Sloan Kettering Cancer Center as part of a thesis submitted to the American Laryngological, Rhinological and Otological Society. This was indeed, one of the largest case series of all times, coming from a center which till date, holds authority in Head and Neck Oncology. It changed the way temporal bone carcinoma would be treated, forever. For the first time in history, meaningful conclusions could be drawn from such an ambient data set. In this landmark paper, the authors brought to attention some basic facts which cannot be overemphasized. An incidence of 1 in 4000 was attributed to neoplasia of middle ear. As per the symptoms, 40 % of patients would present with a history of long standing chronic suppurative otitis media. The authors had performed subtotal resection in 13 patients, 4 of whom were alive after 3 years. Subsequent studies were mostly case series with comparatively much smaller sample size. Needless to explain, we are talking of a disease with such obviously low incidence, that no single center would be a bystander to cases more than a handful. This, in fact, stands true for all cases pertaining to skull base surgery, such that critics would get a chance to comment on the very existence and pertinence of skull base surgery, in the absence of large data sets. Notwithstanding, the remarks have been answered well by the diligent efforts of some eccentric surgeons who dedicated their lives to the development of skull base surgery over decades to come, such that decisions would have the foundation of extravagant data, only if one would care to look into the mist hard enough to make out the strokes of light.

The next large case series was reported by Crabtree et al.[95] in 1976, who described their results of 35 patients and enumerated the 4 basic factors which underlie successful management of temporal bone malignancy: a) early diagnosis; b) correct evaluation of the extent of disease; c) adequate surgery based upon accurate evaluation and d) postoperative radiation in selected cases. These 4 basic principles hold true till this contemporary era of skull base surgery. The very next year, Gacek and Goodman,[96] from Boston, Massacheusets, presented a wonderful account of 31 patients in a highly systematic study, where results were categorised as per the type of surgery. The treatment and outcomes were organised into standardized surgical techniques – Lateral (LTBR), Subtotal (STBR) or Total (TTBR) temporal bone resection. This and all other initial reports showed a survival for temporal bone resection less than 2 years. However, one could also say that the survival was more than one year. It all depends upon human perception, whether "It is half glass full or half glass empty", though a more detailed discussion on this topic will follow in the later part of this manuscript. It's a pity to notice that it takes a lifetime of dedication and perseverance for a surgeon to show results for a technique, yet deserve to be remarked upon by some people standing on the seashore, who have the faintest idea of what the storm was like in the heart of the sea, when the night was dark and hope was meagre.

Talking of a different continent, Yamada et al.[97] described enbloc subtotal temporal bone resection for cancer of external ear, thus describing the early account of surgical management from the neurosurgical perspective. This paper paved the pathway for a string of studies which would appear over the following 2 decades. Four years later, Sasaki,[98] described the intricate details and importance of cerebral veins in otologic surgery, emphasizing on the importance of Vein of Labbe. However, some of the most important landmark studies were published by an Indian neurosurgeon working in North America – the legendary Laligam Sekhar. In 1986,[99] he described the operative exposure and management of petrous and upper cervical internal carotid artery. Four years later, in 1990,[100] he published his work on saphenous vein graft bypass of the cavernous internal carotid artery. 1n 1991,[101] he presented his well known work on combined resection for intracranial extension of cranial base tumours from a neurosurgical prospective, as part of an invited book chapter. As questions remained unanswered with regards to the feasibility and extent of resection for temporal bone tumours, Sekhar et al.[102] presented a case series of 20 patients, reporting the technical advances leading to total resection of tumours in the region of petrous apex, previously considered inoperable due to involvement of dura, brain, petrous ICA, the vein of Labbe, clivus and cavernous sinus. Over a median follow-up period of 30 months, 10 patients with slow-growing malignancies and benign tumours fared well, 7 being alive and disease free. The other 10 patients with fast-growing

malignancies fared poorly, only two being alive without recurrence. In these two patients, the disease was confined to the petrous bone. As a correlation, most of the advanced malignancies reported in various case series on temporal bone neoplasms, are usually confined to the petrous bone.

If to comment on robust data for decision making, it would be pertinent to mention the first systematic review that appeared in the literature, whereby Prasad and Janecka[36] succeeded in a Herculean task, presenting a compilation of all studies published till 1994, leading to specific inferences towards treatment protocols, answering key questions regarding treatment decisions and giving direction to future research. This extensive study presented overall survival outcomes from a large pool of 26 selected articles, as per the technique of resection employed, i.e. – LTBR, STBR or TTBR, apart from stratification of outcomes on the basis of staging of disease as T1 to T4. The intent of this work was to answer 5 key questions – 1) What is the survival of patients with lesions confined to the auditory canal, treated by surgical resection and what type of operation should be performed in this instance? 2) Once the disease enters the middle ear, what is the operation that provides optimal survival? 3) Is Total temporal bone resection ever indicated? 4) How does prognosis change when structures such as the dura mater, brain and internal carotid artery become involved? Is there a role for surgery in these instances? 5) Does the addition of preoperative or postoperative radiation therapy enhance survival?

In relation to the first two questions, well defined inferences could be drawn. There was no statistically significant difference in survival outcomes between mastoidectomy, lateral TBR or subtotal TBR when the disease was confined to the external canal. In cases where the disease involved middle ear, patients who underwent subtotal TBR exhibited a 5-year survival of 41.7% against those who had lateral TBR, demonstrating a 5-year survival of 28.7%. This difference was statistically significant. Apart from this, there was a trend towards lower survival for patients undergoing a mastoidectomy, compared to those who underwent a subtotal TBR. Regarding the last three questions, the authors carefully concluded that the amount of data available to draw any meaningful inferences is too small because the number of patients reported to undergo Total TBR or radical surgery with resection of dura mater or temporal lobe, is insufficient and well formulated clinical trials would be required to answer these critical questions in the future. Also, no homogenous studies were available to describe the role of radiotherapy.

As every work must have a well-defined purpose, the current study should focus on bringing out relevant data in relation to these last three questions, apart from highlighting other important dilemmas such as the controversy of enbloc versus piecemeal resection, the recent revelations and controversies of prognostic factors, reasons for recurrence of disease and the outcomes of multicenter trials. As the purpose of a systematic review should be to present findings in an unbiased manner, the author will make every attempt to present both sides of the debate. In their recent paper in 2014, Prasad et al,[103] have tried to address the questions once again, but an interpretation of the present, more recent review of literature, including studies outside English language literature, suggests that most of the authors have agreed upon lack of sufficient data in relation to Total temporal bone resection and involvement of internal carotid artery. Hence, the topic will be discussed in light of currently available evidence in a neutral manner, trying to bring out the relevant facts, without overemphasizing on opinions of any single author. Also, the most common weakness of most systematic reviews is restricting search to English language literature, which has been surpassed in this present systematic review. The recent publication of a study by Back et al.[104] in 2018, which was a multicenter systematic review and meta-analysis, has opened the topic to discussion once more. This study will be discussed further ahead in this paper.

Considerable confusion exists in the literature regarding the use of term Total temporal bone resection (Total TBR). Though some authors have mentioned that the procedure in its classical form entails sacrifice of interal carotid artery (ICA) for enbloc resection, most authors reporting cases of Total TBR have used this term in relation to Total petrosectomy without sacrifice of ICA. Graham et al,[105] in 1984, published the first study in English language literature which described the total enbloc resection of temporal bone with carotid artery, for malignant tumours of the temporal bone, in a single stage surgery. It is painful to notice how the results of this study have been often undermined by misinterpretation, such that its value has been pathetically underestimated. Different authors have cited this landmark work, only to cloud the picture further by their personal judgements and favouritism, so much so that I am contrived to comment that one must study this paper to understand its real inference. These authors dared to perform Total TBR with carotid artery sacrifice, in a time when such an act would raise a hue and cry, only to bring shame and utmost disgrace to the operator. Clearly, they were ahead of their times, but in the very beginning of this "masterpiece" manuscript, they emphasise on the importance of a specialised skull base team, trained and experienced in skull base surgery, as a separate speciality. In striking detail, they described the nuances of the intracranial intradural part of the technique, along with ways to prevent complications. Two patients, underwent the surgery in a planned manner, operated by a team of neurosurgeons, head and neck surgeons and neurotologic skull base surgeons. The authors concluded that quality of life following this procedure is adequate and the cosmetic deformity can be minimised. As for any other new surgical technique, the surgical procedure had

been established for future reference, in the best manner possible. The only impetus required further is the assessment of results for this technique on lines of long term outcomes and larger sample size to generate adequate data for evidence based practice. Why then the pioneers should be burdened with all the work, while it is the duty of the subsequent generations to carry the flame of elders. However, the development of adequate research grounds in this field has been hampered by opposition from other factors, much like the development of partial laryngectomies has been retarded by disgraceful remarks. Later in 1987, Sataloff et al.[106] presented results from two additional cases, suggesting many modifications in the surgical technique to address the pitfalls. Also, a new procedure was proposed to assure the adequacy of contralateral venous flow. The very next year, Sataloff,[107] presented a detailed account of the procedure, leaving no stone unturned. Perhaps anyone who would spare the time to study this article, would have no doubt about the relevance of this procedure. The author, by metaphorism, compared the procedure of Total TBR to pelvic exenteration, making the ever convincing remarks – "This is not an operation anyone would like to have, but it is sometimes the only alternative to death". The author further contemplated that the procedure requires a team effort, where every member of the team must appreciate the need of this procedure and contribute towards meticulous preoperative, intraoperative and postoperative care. Only then could there be an improvement in the outcomes and rehabilitation for this surgical procedure. Then again, some critics would remark – "Let's talk of relevant data rather than personal opinions and statements". More than five studies were published after Sataloff's initial work on Total TBR. Arriaga,[32] Austin,[35] Hashi,[44] Stankovic,[108] Moody,[3] Kunst,[61] and Lobo,[62] presented 6, 2, 5, 2, 5, 3, and 5 cases of Total TBR respectively (Table 4). Manolidis et al,[42] presented results of 12 cases of Total TBR in a single large study on lateral skull base malignancy.

However, if one were to speak of a study exclusively devoted to outcomes of Total TBR, it was Wu and Wang.[109] who presented the long term outcomes of Total TBR, way back in 1984. In every sense that can be imagined, this work was impeccable, such that these exemplary surgeons had surpassed the times that they lived in, only to be compared to the work of Gregor Johan Mendel in Genetics, who had laid foundations for a new path, 200 years before someone could realise its importance. In an era, when there was nothing more than chisels and curettes available to carry out the surgery, these extravagant surgeons dared to conduct a study on Total Temporal Bone Resection, presenting the long term outcomes for a large number of 22 cases, the greatest ever mentioned in the literature. The patients were operated over a time period from 1961 to 1980. These fine men presented meticulous details in this landmark study, which unfortunately lacks mention in most of the reviews published on this topic. This was ten years after the authors presented their initial report on Total TBR in 1974.[110] According to the UICC Staging followed in that era (1978 UICC classification), 5 patients had stage III disease and 17 suffered from stage IV disease. Five patients underwent primary surgery while 17 cases represented recurrence following radical mastoidectomy, radiation therapy and chemotherapy. Only in such a large sample size, one can be fortunate enough to witness the entire spectrum of survival outcomes. 10 patients (45.5%) never had a recurrence following surgery. At the last follow up, 6 had lived more than 17 years, two for 16 years, two for 15 years, three for 13 years and two for 2 years. Also, to comment on the quality of life and postoperative morbidity, all of these 10 patients resumed their normal work within 6 to 12 months postoperatively. 9 patients (40%) suffered from recurrence, such that four lived for 2 to 3 years, while 5 died within 9 to 12 months. It can be inferred that 14 patients (63.63%) had a survival of more than 2 years. In the 5 patients who died within 9-12 months, there was recurrence in the region of petrous pyramid after previous surgery (radical mastoidectomy) followed by radiation and chemotherapy. Talking of an era when CT imaging was not available, some of these recurrences could have been residual disease. In these 5 patients, the malignant lesions not only extended beyond petrosphenoid suture but also involved a large part of dura in middle cranial fossa. In 2 of the five patients, there was destruction of the bony canals of ICA. Thus only two out of 22 patients (9%) had possible involvement of the ICA. It is most important to mention that these authors did not sacrifice the ICA in any of their 22 surgeries.

In this regard, distinction must be made between the cases operated by Total TBR and the cases with involvement of internal carotid artery, as both are not one and the same thing. Total TBR can also be done for advanced tumours which do not invade the internal carotid artery, thus the results of Total TBR should be interpreted as a separate subcategory compared to results for cases with invasion of internal carotid artery (ICA). Discussing the prognosis for stage IV disease, Lobo et al[62] stated that the survival rates are best when radical surgery is performed as a primary treatment for advanced tumours. Survival falls drastically when surgery is employed for cases of recurrence which have been initially treated by non-surgical therapy or less radical partial resections. In their series survival was longest for patients who underwent primary Total TBR for advanced disease, i.e. 105 and 170 months till last follow-up. It is pertinent to comment that the patient with follow-up of 105 months was 75 years of age, when operated. Moody et al[3] never made a distinction whether in their cases of Total TBR there was an invasion of ICA or not. So is the problem with most of the other studies. In the study by Manolidis et al,[42] there was an invasion of ICA by tumour in four cases operated on through Infratemporal fossa C approach. The prognosis in these cases was worse. It is well recognised that the Infratemporal Fossa

C Approach (Fisch C Approach) is an effective and safe procedure but the results of ICA invasion cannot be superimposed to results of Fisch C approach. Same principle applies to Total TBR where the surgical technique has been criticised not taking into account the fact that most of the studies fail to mention if there was an invasion of ICA by tumor. Another more important factor is involvement and enbloc resection of Eustachian tube, rather than resection of internal carotid artery. Mohri et al,[111] published their work on tubal resection for temporal bone malignancy in 1996. The authors described the technique of total resection of Eustachian tube followed by anterior mobilization and securing of internal carotid artery, which prevents spillage from Eustachian tube, apart from providing access for petrous apex resection with protection of internal carotid artery. More recently, Kawahara et al.[60] (2008) presented the long-term outcomes for radical temporal bone resection for lateral skull base malignancies. They included 14 cases of STBR and 3 cases of TTBR. The five-year recurrence-free and disease-specific survival rates were 67.5% and 60.1%, respectively. The rates increased to 100% and 89% respectively, when the surgical margins were negative. Thus, Total TBR has good survival rates if negative margins can be achieved. In this same year, as if a plan of fate, Okada et al,[63] presented the most encouraging results for temporal bone malignancies involving the dura mater and temporal lobe. Total petrosectomy was done in 4 cases, without sacrifice of ICA. The dura was infiltrated in 3 cases while temporal lobe was involved in 2 cases. In patients with invasion of dura or temporal lobe, the disease was resected enbloc to achieve negative margins. Two of the 3 patients with dural involvement (66.67 %) were alive at last follow-up, one for 31 months and the other for 38 months. The patient who died, survived for more than one year, i.e., 13 months. Of the 2 patients with brain involvement, one (50%) survived till last follow-up, for an astonishing period of 119 months. The other died at 13 months. It is pertinent to emphasize that Okada et al carried out test occlusion of sigmoid sinus in their cases, whenever required, a technique well described by Sekhar et al.[112] in 1997, who described saphenous vein graft bypass of the sigmoid sinus and jugular bulb. Subsequently other authors have discussed the details of the technique.[113,114]

Covering the evidence gaps, presenting the latest results in 2017, Back et al.[104] published a systematic review and meta-analysis on sacrifice and reconstruction of common or internal carotid artery in advanced head and neck carcinoma. This was a multicenter study involving some of the renowned centers of head and neck oncology. 24 articles were selected which included 357 patients. The overall perioperative 30-day mortality was 3.6%. Permanent cerebrovascular complications were encountered in 3.6%. Carotid blow-out episodes occurred in 1.4%. The 1-year, 2-year and 5-year survival rates varied from 23% to 100%, 0 to 82% and 0 to 49 %, respectively. The 2-year disease free survival varied between 19% and 38%. Moreover, the largest study showed an overall 2-year survival of 82% in the setting of low perioperative neurologic sequelae (3.9%) and mortality rates (1.9%). The authors concluded that common or internal carotid artery sacrifice and reconstruction is a feasible treatment option that can be offered to selected patients.

In this regard, it should be emphasized that the procedure be preceded by balloon test occlusion. In the recent coverage on this topic, Tansavatdi with Paul J Donald and others (2015),[115] presented the results of combined Balloon Test Occlusion (BTO) and SPECT analysis (single photon emission computed tomography) for carotid sacrifice, as angiographic predictors for success or failure. A total of 31 patients were included. All patients who passed the neurologic examination during BTO and SPECT, underwent successful carotid artery sacrifice without neurologic sequelae. Patients who failed the occlusive neurologic examination and / or the SPECT, elected chemoradiation except one patient who underwent a successful carotid bypass graft and carotid resection. The success of carotid sacrifice in patients passing both BTO and SPECT was 100%.

As an inference, it can be concluded that Total TBR with sacrifice of internal carotid artery should be carried out only at centers where BTO and carotid reconstruction are available. The lack of expertise and facility should not be interpreted as poor results of Total TBR. Rather, there should be a critical assessment of the extent of tumour in relation to the decision making process, whether a patient requires STBR or TTBR. Patients requiring Total TBR with sacrifice of ICA should be referred to higher tertiary or quaternary centers where BTO and carotid reconstruction are available, instead of criticising TBR for unfavourable results. Only with such development of Triage system, clinical trials and long term studies would be possible, which could provide meaningful survival data, possibly multicenter, on the outcomes of Total TBR, dural involvement and cerebral parenchymal resection. With regards to dura and brain involvement, it is important to mention the study presented by Sekhar et al as far back as 1986.[116] The authors described operative management of tumours involving the cavernous sinus. Seven patients were operated for malignant and benign tumours. All surgeries were preceded by BTO for case selection. The authors made an authoritative remark "If the tumour has already elevated and thinned the temporal lobe considerably as a result of extensive middle fossa involvement, the sylvian fissure is split and gentle temporal lobe retraction is used to gain exposure. If, on the other hand, the tumour is mostly medially situated and localised to the region of the cavernous sinus, the anterior 4 cm of the temporal lobe is excised, starting in the middle temporal gyrus and sparing the medial temporal lobe structures, in order to prevent postoperative contusion and swelling of the temporal lobe." None of the patients in this study died or suffered a stroke postoperatively. Since then there have been multiple reports in this field by legendary surgeons.

Just to name a few, while it was Laligam Sekhar who was the pioneer in the west, in Europe it was Vinko Dolenc.[117] who developed the subspeciality of cavernous sinus surgery. It is more a matter of availability of expertise rather than results of a single surgical procedure.

On a different perspective, Total petrosectomy without involvement of internal carotid artery (ICA) has favourable well established results, as proved by recent multicenter study from Poland.[118] and case series from Japan.[119,120] Asano et al.[119] described a technique for enbloc temporal bone resection, without sacrifice of the ICA. The results were excellent. More recently, Matoba et al,[120] (2018) have confirmed the validity of enbloc resection for advanced temporal bone malignancy. 25 patients were included. In patients with stage IV tumours, the 2-year overall survival for the surgery group was 80% versus 53.6% for those who underwent radiotherapy alone. The 2-year disease free survival for enbloc resection group was 80% versus 28% for those who underwent radiotherapy alone. Similar results have been confirmed by other authors. Somekawa et al.[121] (1997) presented a case report describing enbloc resection of temporal bone malignancy extending to cranial base. In a 70-year old woman, whose tumour extended to middle and posterior cranial fossae, temporal and retromastoid craniotomies were performed. This was followed by exposure of temporal dura, cerebellar dura, transverse sinus and sigmoid sinus. The temporal and cerebellar dura was opened and transverse sinus was ligated at junction with sigmoid sinus. Subsequently, the tentorial dura was incised, such that the incision extended anteriorly to middle cranial fossa, transecting the superior petrosal sinus. This revealed a wide view of middle and posterior cranial fossae. Cranial nerves VII and VIII were divided in the posterior fossa. However, nerves IX, X and XI were preserved. Following this, bone was drilled in area of carotid canal, towards medial side of internal auditory canal and posteriorly to the jugular bulb. Thence, the temporal bone and soft tissue attachments such as middle and posterior cranial fossa dura and sigmoid sinus were separated from pyramidal apex and clivus. The dural defect was repaired with a free pericranial graft while a rectus abdominis free flap was used to reconstruct the defect left by temporal bone resection. There were no postoperative complications like CSF leak, meningitis or lower cranial nerve damage. The patient did not show any recurrence till 28 months of follow-up, neither were there any problems of swallowing and speech. The authors concluded that with recent developments in skull base surgery and reconstruction, more aggressive enbloc resection of temporal bone malignancy has become feasible. It is pertinent to mention here that the study by Bibas et al.[64] (2008) shows that most of the recurrences occur within the first 12 months after surgery. In this case reported by Somekawa, the patient was disease free at 28 months and should be considered cured of disease for all statistical purposes. It can be inferred that when extensive resections are followed by adequate reconstruction, the results are favourable. The surgical approach was very similar to that described more recently by Shi et al.[122] (2011) who call it the temporal base intradural transpetrosal approach to petroclival region and reported a mortality rate of zero percent for this technique.

Perhaps, one of the most important study was published by Moffat et al.[40] in 1997 who presented their results of extended temporal bone resection for recurrent squamous cell carcinoma as a salvage procedure. Fifteen patients were included. Radical surgery yielded a 5-year survival of 47%. 29% of the survivors had temporal lobe involvement that necessitated a partial excision of the temporal lobe of the brain. The authors concluded that radical surgery combined with postoperative radiotherapy from the outset may lead to much better 5-year survival rates than a partial temporal bone resection (radical mastoidectomy) with radiotherapy. A similar study presented by Masterson et al.[123] (2014) included 14 cases with brain involvement. The 5-year disease specific survival for this group was 37% such that there was no significant difference compared to the rest of the cohort. Lavieille et al.[55] (2005) presented their data on 30 patients to reflect the long term outcomes. At the end of the follow-up period of nine years, complete remission was observed in 64.7% of cases involving primary surgery compared to 23.1% for salvage surgery.

However, as stated earlier in this manuscript, a systematic review should bring out both sides of the debate in an unbiased manner. It is important to mention some reports which have made conflicting remarks about the outcomes of resection of advanced temporal bone malignancy. Gidley et al.[124] suggest that involvement of dura mater and cavernous sinus are associated with poor survival outcomes. Similarly, Zanoletti et al.[83] concluded that though involvement of dura mater is not a contraindication to resection, the prognosis in such cases remains guarded. Ironically yet, Gidley et al.[125] presented the largest ever case series in the history of this disease, comprising 157 patients, well surpassing the number reported by Lewis et al in 1960.[26] In this rather interesting paper, the authors have revealed the improvements in survival rates for this rare malignancy, over decades of progress, such that the 5-year overall survival rate of temporal bone malignancy has increased to 58%, with a comparable 5-year disease free survival of 54.9%.[125] On the contrary, others have argued that involvement of dura mater and brain is not a contraindication to surgery if an enbloc R0 resection can be achieved.[9,126]

Role of Radiotherapy: As mentioned earlier, this was the fifth critical question in Prasad and Janecka's study,[36] on outcomes for surgical management. If one were to review the literature reported from different continents, it gives the impression that there is no general consensus on the role of radiotherapy in management of temporal bone malignancy. However, majority of authors

recommend adjuvant postoperative radiotherapy in advanced temporal bone malignancy (T3-T4).[3,61,70,71,77] Other indications which can be enumerated with a more general agreement include close or positive margins,[3,70,77] intracranial invasion,[69] perineural infiltration,[69,70] vascular invasion,[69,70] regional lymph node metastasis.[69,70] and extracapsular spread.[74] The study by Moffat et al,[56] deserves to be mentioned with special emphasis. The authors recommended radical surgery followed by postoperative RT for advanced stage malignancy of temporal bone. However, about two thirds of cases reported were recurrent tumours rather than primary. Thus, while the role of postoperative RT is well defined for recurrent tumours, the indications for primary malignancies are less well agreed upon. For non-squamous cell malignant and benign pathology, similar criteria have been reported by different authors for various pathologies such as adenoid cystic carcinomas,[127-129] adenocarcinomas,[129] and pleomorphic adenomas.[129] Surgery followed by postoperative radiotherapy is the usual trend, though the debate is unsettled as far as sarcomas are concerned. Different institutions follow different protocols in relation to sarcomas of head and neck.

ENBLOC VERSUS PIECEMEAL RESECTION: While Muelleman et al.[130] suggested that piecemeal resection is a valid technique in expert hands, Dean,[69] and Bacciu,[77] described a combination of piecemeal and enbloc resection for T4 tumours. The problem lies in the fact that it is difficult to determine how bone drilling ensures pathologically free margins or bony margins can be verified intraoperatively. Ito et al.[94] presented a study of 16 patients presenting an evaluation of prognostic factors for carcinoma of external auditory canal (EAC). The authors revealed that extensive bone involvement identified on imaging studies correlated with worse prognosis while extensive soft tissue involvement did not correlate with prognosis. Survival was not influenced by the fact whether a hearing disturbance or otalgia was noted at the first medical examination.

SURGERY OF THE PAROTID GLAND: The incidence of parotid involvement in cases of temporal bone malignancy ranges from 10-62%.[103] Mazonni et al,[82] performed superficial parotidectomy as a prophylactic measure in T1 and T2 cases. Total parotidectomy was performed in cases of anterior growth beyond the anterior wall of the external auditory canal. However, Leong et al,[78] presenting their outcomes of radical surgery and postoperative radiotherapy, suggested that parotid involvement was not associated with poor survival outcomes. More recently, Lee et al,[131] (2018) have provided an extensive review of the topic, suggesting a tailored approach to parotidectomy, in congruence with the staging of temporal bone malignancy and the extent of involvement, recommending a margin of at least 1 cm.

PROGNOSTIC FACTORS: Zanoletti et al,[83] presented an analysis of prognostic factors for temporal bone carcinoma in 41 patients based on univariate and multivariate models. On univariate analysis, factors adversely affecting the prognosis were T staging, lymph node involvement, grading of tumour and dura mater involvement. On multivariate analysis, dura mater involvement was the only independent prognostic variable of disease free survival.

Contrary to this, Leong et al,[78] concluded that parotid involvement, node-positive neck and presence of preoperative facial palsy was not associated with poorer survival outcomes. However, Higgins et al,[93] presented a systematic review, concluding that facial nerve involvement is associated with a poor survival outcome and disease with facial palsy should be classified as T4. In another important study, Xie et al,[84] concluded that patients with parotid gland, TMJ involvement and previous middle ear surgery for chronic otitis media had poor survival outcomes. Ito et al,[94] brought out one of the most important facts regarding decision making. The study showed that extensive bone erosion correlates with a worse prognosis of squamous cell carcinoma of temporal bone but extensive soft tissue involvement does not correlate with prognosis.

MULTICENTER STUDIES: Wierzbicka et al,[118] (2017) have recently published results of a multicenter study, comprising of 89 patients from four tertiary referral centers, to present outcomes of extensive surgery: lateral, subtotal and total petrosectomies in patients with temporal bone invasion from specific primary malignancies. The authors proposed that petrosectomy is an effective treatment for malignant temporal bone invasion. Survival outcomes decrease with high T grade, positive margins and salvage surgery while younger age is correlated with better prognosis. It must be mentioned that in this series total petrosectomy was performed without sacrifice of internal carotid artery, revealing excellent outcomes.

CONCLUSION

Long term outcomes for surgical management of temporal bone malignancy have shown a paradigm shift due to improvements resulting from the development of skull base surgery.

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