Management of Acute Complicated Mastoiditis

A Systematic Review and Meta-analysis

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Background: The objective of our study was to evaluate the efficacy of treatment options for the most frequently reported complications of acute mastoiditis in the English literature. PubMed, EMBASE, and The Cochrane Library were searched from database inception through March 29, 2019.

Methods: Two independent reviewers (M.R.K., K.S.) evaluated search results for study inclusion. References cited in publications meeting inclusion criteria were reviewed. Twenty-three included studies were published from 1998 through 2018. Treatment efficacy was determined by comparing the change in number of complication subtypes in each treatment subgroup (medical, conservative, or surgical) from admission to discharge (range: 5–30 days) or postdischarge follow-up (range: 1–27.5 months) with a random effects model.

Results: Among 733 identified articles, 23 met inclusion criteria. Of the 883 included patients, 203 were managed medically (23%), 300 conservatively (34%) and 380 surgically (43%). Conservative patients had more extracranial complications (ECC, $P = 0.04$) and intratemporal complications (IT, $P = 0.04$) at follow-up compared with medical patients. Medical patients had more total number of complications (TNC, $P = 0.03$), ECC ($P = 0.02$), and IT ($P = 0.01$) at discharge compared with surgical patients. Conservative patients had more of all complications except intracranial/extracranial abscess and "other" at discharge and follow-up compared with surgical patients.

Conclusions: There were larger reductions in TNC, ECC, and IT at discharge and follow-up among surgical patients compared with medical and conservative patients. There were greater reductions in TNC, ECC, IT, intracranial complications, subperiosteal abscess and lateral sinus thrombosis at discharge and follow-up among surgical patients compared with conservative patients.

Key Words: mastoiditis, mastoidectomy, antibiotics, complications, treatment outcome

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Acute mastoiditis (AM) is a complication of acute otitis media (AOM). AM occurs when AOM travels from the middle ear to the mastoid air cells through the *aditus-ad-antrum* obstructed by inflammation, pus, or necrotic or granulation tissue. Suppurative disease can lead to abscess formation and subsequent osteonecrosis in severe cases, the latter of which is visualized by loss of trabecular bone on computed tomography and termed "coalescent mastoiditis."[1] Clinically significant suppurative disease presents as fever, postauricular tenderness, postauricular erythema, postauricular edema, and auricular proptosis.[1,2] Expeditious management is crucial because complications can develop rapidly and unexpectedly, including facial nerve palsy, meningitis, intracranial abscess, lateral sinus thrombosis, Bezold's abscess, and acute petrositis.[3] Reported AM complication rates range from 7% to 35%,[4–7] with intracranial complication (ICC) rates affecting an estimated 4%–7% of AM cases.[8–10]

AM management remains controversial. Treatment is often based on institutional guidelines or treating physician or surgeon preference. Generally, the management of AM secondary to AOM warrants inpatient intravenous antibiotics with adequate blood-brain barrier penetration and activity against *S. pneumoniae*, multidrug resistant *S. pneumoniae* and *H. influenza.*[11,12] If AM cases are secondary to CSOM without cholesteatoma, antibiotics should also cover Gram-negative aerobes, *Pseudomonas spp.*, methicillin-resistant *S. aureus*, and *S. aureus.*[11,12] If medical management fails or if AM cases are secondary to CSOM with cholesteatoma, patients are managed surgically with the goal of debriding infected or necrotic tissue and restoring tympanic and mastoid aeration.[13,14] A 2019 meta-analysis by Anne et al reported a 75% cure rate among medically managed pediatric AM patients and a near-100% cure rate among surgically managed pediatric AM patients.[2] This study defined mastoiditis cure based on patient condition at the time of discharge with an exclusive focus on pediatric populations. Our study aims to broaden this investigation by studying the efficacy of mastoiditis treatment strategies among complicated AM patients stratified by subgroup with treatment outcome assessed at the time of hospital discharge and postdischarge clinical follow-up. It is the most comprehensive analysis to date to investigate the management of complicated AM.

MATERIALS AND METHODS

Inclusion Criteria

Retrospective studies, retrospective chart/literature reviews, and retrospective case series of patients with acute complicated mastoiditis (ACM), defined medical, conservative, or surgical management, defined ACM complications, record of clinical condition at admission, discharge, and postdischarge follow-up, and ACM complications defined by management strategy and follow-up time were included.

Exclusion Criteria

Studies that did not have mastoiditis as a clinical diagnosis, did not have defined subgroup allocation to medical, conservative, or surgical management with defined medical, conservative, or surgical management, or did not have pretreatment as well as

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posttreatment or follow-up complications linked to each subgroup were excluded. Studies describing patient clinical condition at the time of discharge without postdischarge follow-up were included and noted as having a clinical follow-up time of "0."

Eligibility Criteria

We searched MEDLINE, EMBASE, and The Cochrane Library from database inception through 2019 using the following terms: "'mastoiditis' and 'antibiotic' OR 'antimicrobial' OR 'antibacterial' OR 'anti-infective' OR 'medical' OR 'conservative' OR 'nonsurgical'" and "'surgery' OR 'perioperative period' OR 'postoperative period' OR 'preoperative period' OR 'mastoidectomy' OR 'middle ear ventilation' OR 'myringotomy' OR 'tympanostomy tube' OR 'grommet' OR 'retroauricular puncture' OR 'pressure equalization' OR 'mastoidectomy' OR 'tympanomastoidectomy' OR 'mastoid surgery' OR 'surgery' OR 'surgical' OR 'operative.'" Non-English language papers and duplicates were excluded. A systematic title review was conducted by 2 reviewers (M.R.K., K.S.) who independently agreed upon articles for inclusion in the meta-analysis with 1 reviewer (M.R.K.) extracting data for data analysis. Additionally, references cited in publications meeting search criteria were searched. Data items extracted from each study were defined before the literature search as follows: study country and publication year, study subtype, the number of patients, mean patient age at admission, sex, the number of patients with preadmission antibiotic treatment (when available), bacterial culture rate, and bacterial culture results. The total number of complications (TNCs), ICCs, ECCs, intratemporal complications (ITs), subperiosteal or retroauricular abscesses (SPAs), lateral sinus thromboses (LSTs), extracranial thromboses, intracranial abscesses (IAs), non-SPA extracranial abscesses, and "other" complications were recorded for each study at the time of admission, discharge, and postdischarge follow-up times grouped by AM management strategy (medical, conservative, or surgical) performed. ICCs were those within the cranial cavity and were defined as cerebral venous sinus thromboses, IAs, meningitis, and other complications. ECCs were defined as those complications outside the cranial cavity and included extracranial thromboses, extracranial abscesses that were not subperiosteal abscesses, or other systemic complications. Intratemporal complications were defined as subperiosteal abscesses and retroauricular abscesses. Medical management included inpatient intravenous antibiotics, conservative management as previously defined by Psarommatis et al[15] included myringotomy ± tympanostomy tube placement (MT), and surgical management consisted of abscess drainage or mastoidectomy.

Risk of Bias Assessment

Studies meeting inclusion criteria were assessed for bias with the final, revised, and validated Methodological Index for Non-Randomized Studies (MINORS) scale.[16] This 12-item bias assessment tool rates each nonrandomized study quality as 0 (not present), 1 (reported but inadequate), or 2 (reported and adequate). The first 8 items are used to score both noncomparative and comparative studies. The last 4 items are exclusively used to score comparative studies. Noncomparative studies were scored a maximum of 16 points and comparative studies were scored a maximum of 24 points.

Statistical Analysis

Study and patient characteristics were described as pooled point estimates and presented as mean, median, and range for continuous variables and as frequencies or proportions for categorical variables. Chi-square tests of association were conducted to assess the degree of association or independence of 2 categorical variables. One-way analysis of variance (ANOVA) testing was conducted to assess for significant differences between 1 independent variable composed of ≥3 categorical, independent groups, and 1 continuous dependent variable.

The standardized mean difference and its 95% confidence interval (CI) were estimated for each study included in the meta-analysis. Analyses were conducted separately for each complication among the 3 AM management strategies (medical, conservative, and surgical). Only studies with specified patient management strategy and complication type were included for meta-analysis. The change in pretreatment number of complications was assessed at posttreatment or follow-up. A treatment arm continuity correction method was applied to observations containing zero reported events for a given complication.[17] Cochran's Q testing was used to evaluate heterogeneity across studies, and I^2 was calculated to describe the variation due to heterogeneity rather than to chance between studies.[18] Because heterogeneity was observed, we applied a Dersimonian and Laird[19] random effects model to calculate the overall standardized mean difference and its 95% CI for the complications studied. Publication bias was assessed with Bregg's and Egger testing and funnel plot asymmetry. Analyses were conducted in STATA (version 15.1).[20] Statistical significance testing was two-tailed, using an inference threshold of $P < 0.05$.

RESULTS

Seven hundred thirty-three full-text articles of level IV evidence met inclusion criteria for final review and data extraction, 710 of which were excluded from further analysis (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/E637). Reasons for exclusion included: lack of management subgroup allocation (70%), lack of reported complications at pretreatment and discharge, or follow-up within management subgroups (24%), and no mastoiditis diagnosis (0.8%). Among the 23 included studies, 16 were retrospective literature or chart reviews and 7 were retrospective case series.

Study Characteristics

Twenty-three included studies were published from 1998 through 2018 (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/E638)[7,15,21–41]. The majority of studies were conducted in the United States (22%) and Israel (22%). Mean patient follow-up time was 6.2 months.

Patient and Clinical Characteristics

Patients averaged 4.5 years of age at the time of admission (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/E638) with a significant male predominance (59.4%, $P = 0.007$). Among all patients studied, 37.8% were initially managed with surgery. There were no significant differences in the number of patients allocated to each of the 3 management strategies at initial presentation ($P = 0.11$). 74.8% of patients had positive bacterial cultures, 57.3% of which had *S. Pneumoniae* and 44% of which had SPA.

Complications

There were a total of 833 patients. 192 were managed medically (23%), 283 conservatively (34%), and 358 surgically (43%) (**Table 1**). All comparisons were significantly heterogeneous ($I^2 > 50\%$ and Cochrane $Q < 0.05$). The comparison between conservative and surgical management had the most publication bias.

Medical Versus Conservative Management

There were 6 studies with medically and conservatively managed patients evaluated at admission, discharge, or follow-up with

TABLE 1. Overall Random Effects Model Summary*

	Admission to Discharge				Admission to Follow-up			
	No. of studies	SMD	95% CI	*P*	No. of studies	SMD	95% CI	*P*
Medical vs. conservative management								
Total number of complications	6	–0.525	[–3.976, 2.926]	0.765	6	1.487	[–0.639, 3.613]	0.170
Extracranial complications	6	1.267	[–0.915, 3.450]	0.255	6	–1.218	[–2.406, –0.031]	0.044
Intratemporal complications	6	1.162	[–0.994, 3.318]	0.291	6	–1.218	[–2.406, –0.031]	0.044
SPA	6	–0.592	[–1.291, 0.108]	0.097	6	–0.983	[–2.103, 0.137]	0.085
Medical vs. surgical management								
Total number of complications	5	7.171	[0.608, 13.734]	0.032	5	2.33	[–3.010, 7.671]	0.392
Intracranial complications	5	0.869	[–0.624, 2.361]	0.254	5	0.856	[–0.621, 2.334]	0.256
Extracranial complications	5	6.334	[1.137, 11.531]	0.017	5	1.581	[–1.998, 5.160]	0.387
Intratemporal complications	5	5.863	[1.222, 10.504]	0.013	5	1.308	[–2.067, 4.683]	0.448
SPA	5	2.164	[–0.912, 5.239]	0.168	5	1.308	[–2.067, 4.683]	0.448
CVST	5	0.446	[–0.237, 1.128]	0.201	5	0.442	[–0.237, 1.121]	0.202
Intracranial Abscess	5	0.459	[–0.533, 1.450]	0.364	–	–	–	–
Other	4	0.466	[–0.206, 1.139]	0.174	–	–	–	–
Conservative vs. surgical management								
Total number of complications	14	15.373	[10.747, 19.999]	0.000	13	6.349	[3.326, 9.372]	0.000
Intracranial complications	14	1.859	[0.581, 3.136]	0.004	13	1.819	[0.545, 3.092]	0.005
Extracranial complications	14	10.539	[7.366, 13.712]	0.000	13	5.127	[2.344, 7.910]	0.000
Intratemporal complications	14	10.068	[6.968, 13.168]	0.000	13	4.734	[2.011, 7.457]	0.001
SPA	14	5.103	[2.428, 7.777]	0.000	13	4.589	[1.934, 7.243]	0.001
CVST	14	0.973	[0.228 1.719]	0.01	13	0.869	[0.152, 1.587]	0.018
Extracranial thrombosis	–	–	–	–	13	0.019	[–0.147, 0.185]	0.825
Intracranial Abscess	14	0.689	[–0.293, 1.671]	0.169	13	0.678	[–0.298,1.655]	0.173
Extracranial abscess (non-SPA)	14	0.056	[–0.110, 0.222]	0.511	13	0.055	[–0.111, 0.221]	0.516
Other	5	0.134	[–0.137, 0.405]	0.332	5	0.19	[–0.092, 0.472]	0.187

*Results depict the standardized mean difference (SMD) for complications by management strategy on admission. Subgroup regression analyses with zero applicable studies or patients are omitted from this table or left blank, denoted as "–."

CVST indicates cerebral venous sinus thrombosis; Other, includes periorbital cellulitis (2 patients), otitis hydrocephalus (4 patients), CN VI palsy (2 patients), intraoperative shrapnel cholesteatoma (2 patients), Gradenigo syndrome (2 patients), mild thrombocytopenia in the setting of recent heparinization, postoperative wound cellulitis (2 patients), postoperative bleeding or hematoma (4 patients), recurrently elevated intracranial pressure (1 patient), epilepsy/developmental delay (1 patient), persistent headaches (2 patients), high-frequency sensorineural hearing loss (1 patient); SPA, subperiosteal abscess.

mastoiditis complicated by ECC, IT, or SPA. There were no significant differences in TNC, ECC, IT, or SPA at discharge between medically and conservatively managed patients. However, conservatively managed patients had significantly more ECC ($P = 0.04$) and IT ($P = 0.04$) at follow-up relative to medically managed patients (**Table 1**). There was no significant publication bias.

Medical Versus Surgical Management

There were 5 studies with medically and surgically managed patients evaluated at admission and discharge with mastoiditis complicated by ICC, ECC, IT, SPA, LST, IA, or "other." Patients evaluated at admission and follow-up had ICC, ECC, IT andSPA. Medically managed patients had significantly more TNC ($P = 0.03$), ECC ($P = 0.02$), and IT ($P = 0.01$) at discharge compared with surgically managed patients (**Table 1**). There were no significant differences in TNC, ICC, ECC, IT, or SPA at follow-up between medically and surgically managed patients. There was no significant publication bias.

Conservative Versus Surgical Management

There were 14 studies with conservative versus surgically managed patients evaluated at admission and discharge with mastoiditis complicated by ICC, ECC, IT, SPA, LST, IA, or non-SPA extracranial abscess. 13 studies had patients with "other" evaluated at admission and discharge. There were 13 studies of patients evaluated at admission and follow-up with ICC, ECC, IT, SPA, LST, IA, extracranial thrombosis, non-SPA extracranial abscess, and "other." Conservatively managed patients had significantly more TNC, ICC, ECC, IT, SPA, and LST at discharge and follow-up compared with surgically managed patients (**Table 1**). There was significant publication bias when comparing TNC at admission versus discharge, ECC and SPA at admission versus follow-up, and IT at admission versus discharge and follow-up ($P < 0.05$).

DISCUSSION

Our study investigated mastoiditis treatment efficacy defined by complication at the time of hospital discharge and postdischarge follow-up. ICCs included LST, IA, and meningitis. Common ITs included SPA. There were more than twice as many ECCs than ICCs. The most common overall complication was SPA. Mastoiditis may frequently involve contiguous involvement of local anatomic structures leading to extracranial manifestations before development of intracranial complications, but a prior study investigating patients with intracranial complications demonstrated that many patients presented without signs of otorrhea or subperiosteal abscess.[42]

Similar to other studies, there was a slight predominance of males to females of 59.4% with prior studies ranging from 55% to 69%.[1,11,43,44] Almost half of patients who presented with mastoiditis had been on a prior treatment with antibiotics. As prior investigations have concluded, it is challenging to determine the efficacy of outpatient therapy as patient compliance, length of antibiotic course before inpatient admission, and choice of antibiotic could have a large impact on the improvement in clinical symptoms overall and subsequent development of complications. Prior studies have demonstrated that antibiotic treatment is not necessarily preventative for mastoiditis and its complications, although it may reduce the risk in certain populations.[4–6,8]

Consistent with results from Anne et al,[2] surgical treatment had the highest cure rates for total complications and individual complications, whether surgery was performed during the same admission or at follow up. The exceptions were when compared with intravenous treatment with antibiotics for intracranial complications or when compared with medical or conservative management for IAs. Our results demonstrating an increase in intracranial complications in the surgical management group between discharge and follow-up mirror those of Mallur et al, in which the authors concluded that a protracted course of antibiotics may be sufficient in management of intracranial complications of mastoiditis.[7] Ultimately, management of IAs are often complex and require a calculated pharmacologic and surgical approach often formulated by an interdisciplinary collaboration.[3] Medical management appears to be better at reducing the number of complications at follow up when compared with treatment with conservative measures in follow up patients with extracranial or intratemporal complications. Based on included studies, surgery is performed more frequently than other treatment options, although still in less than half of cases in patients presenting with complications. There were differences among institutional management of ACM, ranging from "graded" management based on complication subtype and intravenous antibiotic responsiveness to more aggressive management with immediate surgical intervention. These differences were accounted for in our preanalytic risk of bias assessment, heterogeneity testing and random effects meta-analysis modeling.

A study by Quesnel et al[44] recommended an AM management algorithm utilizing a trial of IV antibiotics for 48 hours with surgery reserved for those with clinical and biologic failure with this treatment. Psarommatis et al[15] proposed an algorithm for mastoiditis with SPA and suggested a trial of myringotomy and drainage with mastoidectomy reserved for patients deemed to have a poor response to this initial management after a few days. For suspected intracranial complications, myringotomy plus mastoidectomy was utilized with good results in their study. Various studies have concluded that various levels of difference in outcomes in patients presenting with AM with SPA who are managed with incision and drainage ± antibiotics/tympanostomy versus mastoidectomy with reports of no difference[45,46] to 42.9% of patients requiring a subsequent mastoidectomy due to failure to improve.[15] Discrepancies with our results may partially be accounted for by the presence of concurrent complications in patients with SPA or the addition of follow-up data which could account for reemergence of complications with more conservative treatment approaches.

Our findings suggest that there is a role for triaging patients presenting with AM with complications with preference for surgical intervention to abscess drainage or mastoidectomy early for this subgroup of patients rather than a trial or wait and see approach with more conservative measures. Additionally, in cases with just intracranial complications secondary to mastoiditis, treatment with intravenous antibiotics could be beneficial before surgical management.

Surgical management of mastoiditis is not without its drawbacks, requiring prolonged general anesthesia, further surgical complication risks, increased resource utilization, and enhanced morbidity. However, in select cases with patients who present with complications, it may be a more viable option in ensuring patients have reduced posttreatment and follow-up complications relative to medical or conservative management.

Ultimately, the decision to undergo surgery for mastoiditis is multifactorial. Although the mortality rate is extremely low overall, increased patient morbidity and length of hospital stay are important considerations that are important to patients. Individual patient characteristics that were not accounted for in studies analyzed such as underlying comorbidities, severity of complications, expediency of treatment, and compliance through follow up are also a few of the potential measures which may further dictate individualized treatment. There was also insufficient individualized patient data to determine the differences in in benefit between surgical management with abscess drainage and mastoidectomy and discretion should be on a case-by-case basis.

There were also limitations to our study, many which were controlled as much as possible. Selection bias was minimized by having 3 separate authors (M.R.K., K.S., A.S.) perform a full literature review and reach consensus on included and excluded studies. The statistical methods employed in this meta-analysis also helped to control for bias. We employed an intention-to-treat analytic approach, wherein patients were analyzed according to their initial intended treatment group regardless of any subsequent treatments they eventually received (eg, a failed medically managed AM patient who underwent subsequent surgical intervention). Publication bias was objectively assessed with Bregg's and Egger testing and funnel plot asymmetry.

Unfortunately, there was not sufficient sample number to make comparisons on treatment of every complication included in our meta-analysis. We controlled for this with inclusion of the MINORS scale and heterogeneity testing. Additionally, there is a paucity of data collected from randomized controlled trials and results were collected predominantly from case series and retrospective reviews. To test the quality of the studies included, the MINORS scale was utilized due to the inclusion of nonrandomized comparative and noncomparative studies in our analysis.[16]

CONCLUSIONS

There were larger reductions in TNC, ECC, and IT at discharge and follow-up among surgical patients compared with medical and conservative patients. There were greater reductions in TNC, ECC, IT, intracranial complications, subperiosteal abscess and lateral sinus thrombosis at discharge and follow-up among surgical patients compared with conservative patients.

For any type of complications, extracranial complications, and intratemporal complications, surgical management at initial presentation is associated with reduced complications at post-treatment and follow-up compared with medical or conservative management. For intratemporal complications and SPA, surgical management reduces complications compared with conservative management.

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