Supplementary Table S1 Inclusion and exclusion criteria

Category	Inclusion criteria	Exclusion criteria
Age	All ages	No age restriction
Patient base	Osteoradionecrosis of the median skull base	Osteoradionecrosis of the lateral the skull base
Treatment	All surgical approaches	No surgical approach excluded
Study methodologies	All study methodologies	No limitation
Study population	Human studies	Animal studies Cadaver studies
Geography	All locations	No limitation
Date of search	January 1990–June 2000	NA
Outcomes	Disease progression Mortality	NA
Publication languages	All languages	No limitation
Publication type	All publications types	No limitation

Abbreviation: NA, not applicable.

Supplementary Table S2 Search criteria

Database searched	Search terms
PubMed/ Medline	Skull base AND osteoradionecrosis
EMBASE	"Skull base" AND ("bone necrosis"/exp OR "bone necrosis") AND "radiation necrosis"
Cochrane library	Skull base AND osteoradionecrosis

Supplementary Table S3 National Institutes of Health study quality overall assessment

Study	Year	Overall score	Study	Year	Overall score
Habib et al[25]	2020	Good	Hu[38]	2013	Poor
Daoudi et al[23]	2020	Fair	Raza[47]	2013	Fair
Ungar[49]	2020	Good	Wang[53]	2011	Poor
Vieira et al[50]	2020	Fair	King et al[41]	2010	Fair
Liu[24]	2019	Good	Kakarala et al[40]	2010	Fair
Chapchay[34]	2019	Fair	Liang et al[42]	2009	Good
Hallak et al[37]	2019	Fair	Huang et al[39]	2006	Good
Vlantis[51]	2018	Fair	Wang[52]	2006	Poor
Huang[22]	2018	Good	Mut[45]	2005	Fair
London[44]	2018	Fair	Liu[43]	2004	Poor
Choi[55]	2017	Fair	Chen et al[35]	2004	Poor
Risso et al[48]	2016	Fair	Chang[33]	2000	Good
Adel and Chang[3]	2016	Fair	Wu and Lee[54]	1999	Poor
Tan[31]	2015	Fair	Ness[46]	1996	Poor
Brand[29]	2015	Poor			

Abbreviation: NIH, National Institute of Health.

Supplementary Table S4 Study quality assessment for before-after studies with no control group

Study	Habib et al[25]	Daoudi et al[23]	Liu[24]	Huan[22]	Liang et al[42]	Huang et al[39]	Chang[33]
Objective clear?	Y	Y	Y	Y	Y	Y	Y
Eligibility/selection criteria prespecified and clear?	Y	Y	Y	Y	Y	Y	Y
Participants representative of intervention-eligible population?	Y	Y	Y	Y	Y	Y	Y
All eligible participants with prespecified entry criteria enrolled?	Y	Y	Y	Y	Y	Y	Y
Sample size sufficient?	Y	N	Y	Y	Y	Y	N
Intervention clear and delivered consistently?	Y	N	Y	Y	N	Y	Y
Outcomes prespecified, clear, valid, reliable, and assessed consistently?	Y	N	Y	Y	Y	Y	Y
Outcome assessment blinded?	N	N	N	N	N	N	N
Loss of follow-up 20% or less? Analysis includes this group?	Y	Y	Y	Y	Y	Y	Y
Statistics measured outcomes before to after intervention? p-value?	Y	NA	Y	Y	NA	NA	NA
Outcomes measured multiple times before and after intervention? Interrupted time series design?	N	N	N	N	N	N	N
Overall score	Good	Fair	Good	Good	Good	Good	Good

Abbreviations: CD, cannot determine; N, no; NA, not applicable; NR, not reported; Y, yes.

Supplementary Table S5 Study quality assessment for case series and case reports (1/3)

Study	Ungar[49]	Vieira et al[50]	Chapchay[34]	Hallak et al[37]	Vlantis[51]	London[44]	Choi[55]	Risso et al[48]
Objective clear?	Y	Y	Y	Y	Y	Y	Y	Y
Population well described?	Y	Y	Y	Y	Y	Y	Y	Y
Cases consecutive?	ND	NA	NA	NA	ND	NA	ND	NA
Cases comparable?	Y	NA	NA	NA	Y	NA	Y	NA
Intervention clear?	Y	Y	Y	Y	Y	Y	Y	Y
Outcomes clear, valid, reliable, and consistent?	Y	N	NA	N	N	NA	N	N
Length of follow-up adequate?	Y	Y	Y	N	Y	Y	Y	N
Statistics well-described?	Y	NA	NA	NA	NA	NA	NA	NA
Results well-described?	Y	Y	Y	Y	Y	Y	Y	Y
Overall score	Good	Fair	Fair	Fair	Fair	Fair	Fair	Fair

Abbreviations: CD, cannot determine; N, no; NA, not applicable; NR, not reported; Y, yes.

Supplementary Table S6 Study quality assessment for case series and case reports (2/3)

Author	Brand[29]	Hu[38]	Raza[47]	Wang[53]	King et al[41]	Kakarala et al[40]
Objective clear?	Y	Y	Y	Y	Y	Y
Population well described?	Y	Y	Y	Y	Y	Y
Cases consecutive?	NA	NA	NA	NA	ND	NA
Cases comparable?	NA	NA	NA	NA	Y	NA
Intervention clear?	Y	Y	Y	N	N	Y
Outcomes clear, valid, reliable, and consistent?	N	N	N	N	Y	N
Length of follow-up adequate?	N	N	Y	N	N	Y
Statistics well-described?	NA	NA	NA	NA	NA	NA
Results well-described?	N	N	Y	N	Y	Y
Overall score	Poor	Poor	Fair	Poor	Fair	Fair

Abbreviations: CD, cannot determine; N, no; NA, not applicable; NR, not reported; Y, yes.

Supplementary Table S7 Study quality assessment for case series and case reports (3/3)
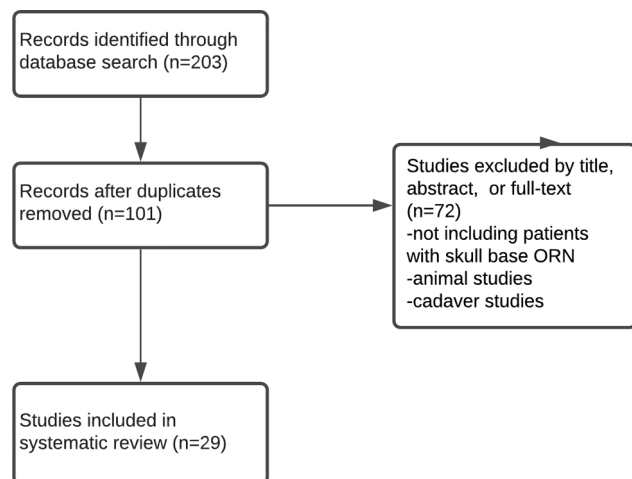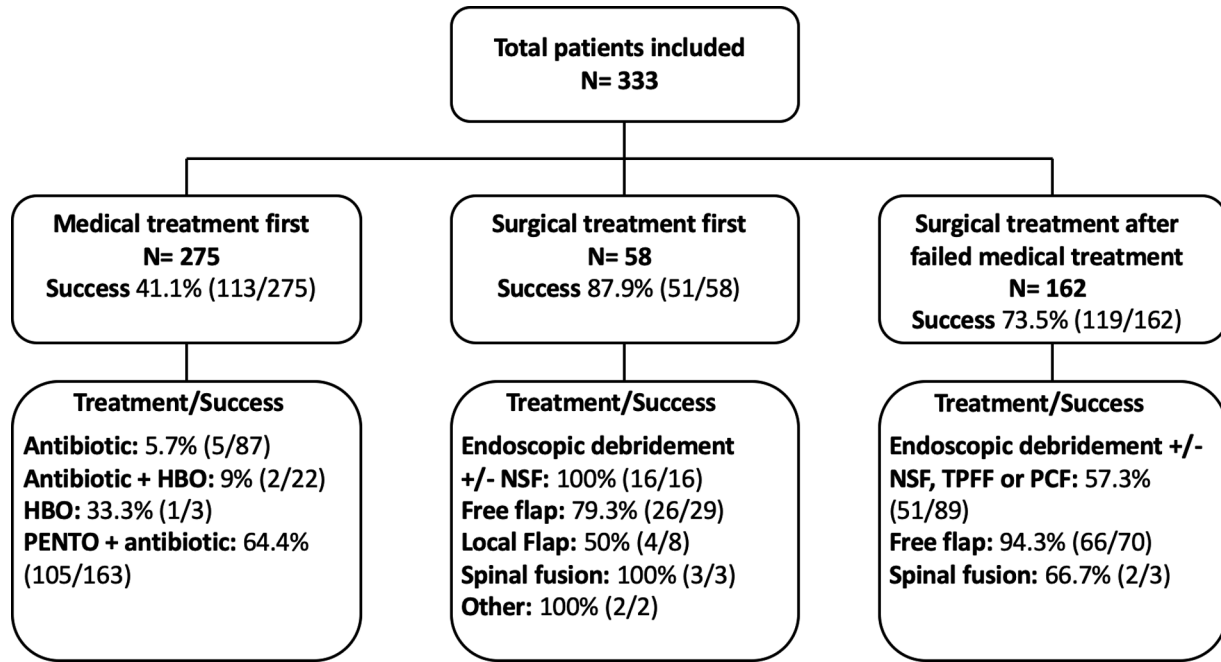
Criteria	Wang[52]	Mut[45]	Liu[43]	Chen et al[35]	Wu and Lee[54]	Ness[46]
Objective clear?	Y	Y	Y	Y	Y	Y
Population well described?	Y	Y	Y	Y	Y	Y
Cases consecutive?	NA	NA	NA	NA	NA	N
Cases comparable?	NA	NA	NA	NA	NA	Y
Intervention clear?	N	Y	N	Y	Y	Y
Outcomes clear, valid, reliable, and consistent?	N	N	N	N	N	N
Length of follow-up adequate?	N	N	N	N	N	Y
Statistics well-described?	NA	NA	NA	NA	NA	NA
Results well-described?	N	Y	N	N	N	Y
Overall score	Poor	Fair	Poor	Poor	Poor	Poor

Abbreviations: CD, cannot determine; N, no; NA, not applicable; NR, not reported; Y, yes.

Supplementary Fig. S1 PRISMA flow chart of study selection process. A total of 203 studies were identified from literature search; 102 studies remained after removal of duplicate studies; 101 articles were excluded after viewing title, abstract, or full-text; and 29 studies were included in the final analysis.

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                    ┌─────────────────────────────┐
                    │   Total patients included   │
                    │          N= 333             │
                    └─────────────────────────────┘
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Medical treatment first N= 275 Success 41.1% (113/275)	Surgical treatment first N= 58 Success 87.9% (51/58)	Surgical treatment after failed medical treatment N= 162 Success 73.5% (119/162)
Treatment/Success **Antibiotic:** 5.7% (5/87) **Antibiotic + HBO:** 9% (2/22) **HBO:** 33.3% (1/3) **PENTO + antibiotic:** 64.4% (105/163)	**Treatment/Success** **Endoscopic debridement +/- NSF:** 100% (16/16) **Free flap:** 79.3% (26/29) **Local Flap:** 50% (4/8) **Spinal fusion:** 100% (3/3) **Other:** 100% (2/2)	**Treatment/Success** **Endoscopic debridement +/- NSF, TPFF or PCF:** 57.3% (51/89) **Free flap:** 94.3% (66/70) **Spinal fusion:** 66.7% (2/3)

Supplementary Fig. S2 Flow chart showing the different treatment arms for the patients included in the analysis. Outcome for each arm is included. HBO, hyperbaric oxygen; PENTO, pentoxifylline-tocopherol; NSF, nasoseptal flap; TPFF, temporoparietal fascia flap; PCF, pericranial flap.