Supplementary Material Legend

Bubenikova A, *et al. J Neurol Neurosurg Psychiatry* 2022; 93:475–480. doi: 10.1136/jnnp-2021-328658

eMethods 1. PICO + Keywords used for literature search + Eligibility criteria

PICO Worksheet	
Population	Patients diagnosed with cerebral cavernous malformations
Intervention	Surgery versus radiosurgery versus observation
Comparison	Not applicable
Outcome	The risk of haemorrhage within each treatment modality

Table 1: The applied PICO worksheet.

Keywords used for literature search:

1. cavernous angioma (natural history or surgery or radiosurgery),
2. cavernous haemangioma (natural history or surgery or radiosurgery),
3. cavernous hemangioma (natural history or surgery or radiosurgery),
4. cavernous malformations (natural history or surgery or radiosurgery),
5. natural history of cavernous malformations,
6. surgery of cavernous malformations,
7. radiosurgery of cavernous malformations.

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Eligibility criteria:

1. 20 patients per study,
2. no specifications on age, gender, rase etc.,
3. both adult and paediatric patients,
4. single study must have been published between January 1990 and December 2020,
5. no specifications on study's design (both retrospective and prospective publications),
6. single study must have presented outcomes of surgical, radiosurgical or conservative treatment (at least one of the mentioned), all studies must have been published in English.

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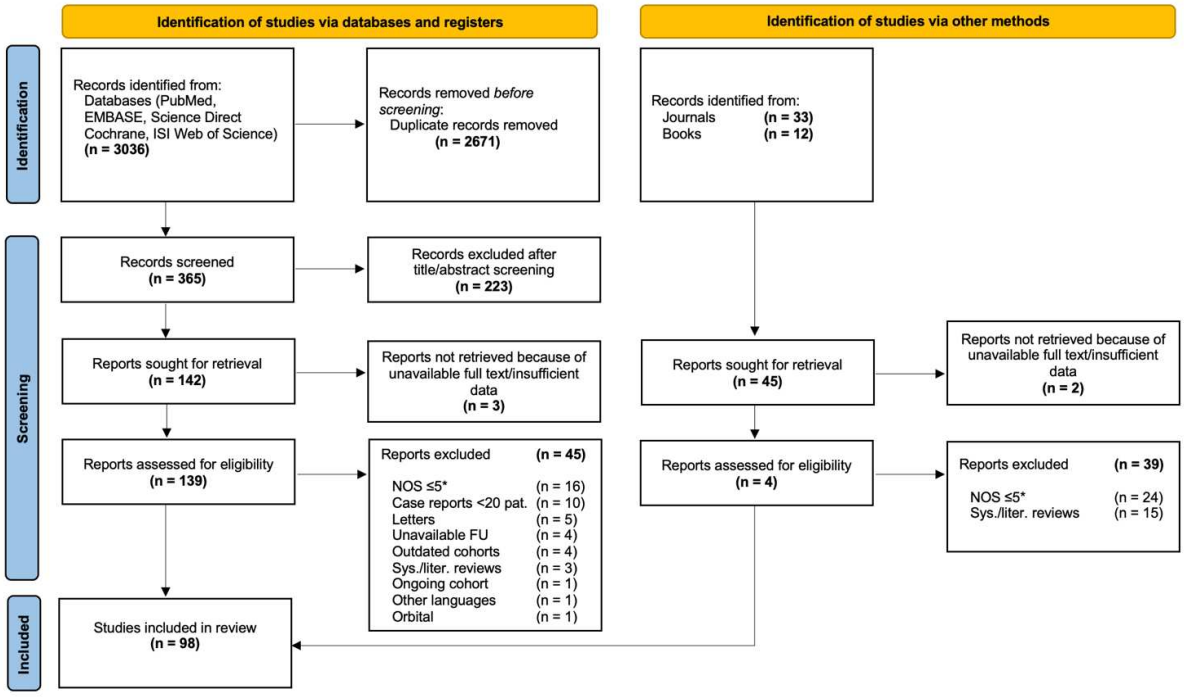
eMethods 2. PRISMA diagram



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Figure 1: PRISMA flowchart.

eMethods 3. Newcastle-Ottawa Scale

NOS quality assessment. We defined the following quality score: "good" quality score by 3 or 4 stars in the selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. Definition of "fair" quality score was defined as 2 stars in the selection, 1 or 2 stars in comparability, and 2 or 3 stars in outcomes. Finally, "poor" quality score was defined by 0 or 1 star(s) in the selection, 0 stars in comparability, and 0 or 1 star(s) in outcomes.

NEWCASTLE-OTTAWA QUALITY ASSESSMENT SCALE

COHORT STUDIES

Selection

1) Representativeness of the exposed cohort

a) truly representative of the average target in the community, i.e., patients diagnosed with cerebral cavernous malformation(s); CCM(s) ✷

b) somewhat representative of the average target in the community, i.e., patients diagnosed with cerebral cavernous malformation(s); CCM(s) ✷

We defined somewhat representatives to be patients diagnosed with CCM(s) who (1) were treated with different comorbidities altogether with CCM(s); (2) were reoperated; (3) underwent more than one invasive treatment approach; (4) all had specific CCM(s), e.g., only brainstem CCMs.

c) selected group of users, e.g., nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non-exposed cohort

a) drawn from the same community as the exposed cohort ✷

b) drawn from a different source

We consider different source to be: (1) specific population of patients (e.g., if some patients were excluded because of their nationality, gender, age etc.); or (2) patients who were derived from a group only consisting of family relatives.

c) no description of the derivation of the non-exposed cohort

3) Ascertainment of exposure

a) secure record such as: surgical record or MRI evaluation ✷

b) detailed clinical and radiological evaluation by specialist blinded to patients' clinical status ✷

c) written self-report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes ✷

We consider this demonstration to be: (1) exclusively defined methods of diagnosis steps; (2) prospective design of the study; (3) prospectively collected patients' records; (4) independent blind assessment in retrospective citations; (5) independent evaluations of postoperative and follow-up data.

b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis

a) study controls for age and sex of individual patients ✷

b) study controls for any additional factor, comorbidity, such as: developmental venous anomaly (DVA), coagulation, CCM size ✷

Outcome

1) Assessment of outcome

a) independent blind assessment ✷

b) record linkage which we consider to be MRI ✷

c) self-report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes ✷

We defined the enough length of outcomes to occur to be mean 3 years with the minimum of 6 months of follow-up per patient.

b) no

3) Adequacy of follow up of cohorts

a) complete follow up — all subjects accounted for ✷

b) subjects lost to follow up unlikely to introduce bias — small number lost — > 20% during follow up, or description provided of those lost ✷

c) follow up rate < 80% during follow-up and no description of those lost

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	Selection				Comparability		Outcome			
Authors + year	**Representativeness of Exposed Cohort**	**Selection of the Non-Exposed Cohort from Same Source as Exposed Cohort**	**Ascertainment of Exposure**	**Outcome of Interest Was Not Present at Start of Study**	**Comparability of Cohorts**	**Assessment of Outcome**	**Follow-up Long Enough for Outcome to Occur (< mean 3 years)**	**Adequacy of Follow-Up**	**Quality Score**	Exclusion
Abla et al. 2011 [1]	1	1	1	0	11	1	0	1	Good	
Acciari et al. 2009 [2]	1	1	0	0	11	0	1	1	Fair	
Agosti et al. 2019 [3]	0	1	1	1	11	1	0	0	Fair	YES
Aiba et al. 1995 [4]	1	1	0	0	11	0	0	1	Fair	YES
Al-Holou et al. 2012 [5]	1	1	1	0	11	1	0	1	Good	
Al-Shahi Salman et al. 2012 [6]	1	1	0	1	11	0	1	1	Good	
Amato et al. 2013 [7]	1	1	0	0	1	1	0	1	Fair	
Amin-Hanjani et al. 1998 [8]	1	1	0	0	11	0	0	1	Fair	YES
Amin-Hanjani et al. 1998 [9]	1	1	0	0	11	1	0	1	Fair	
Arauz et al. 2017 (1&2) [10]	1	1	1	1	11	1	1	1	Good	
Barker et al. 2001 [11]	1	1	0	0	11	0	0	1	Fair	YES
Bartolomei et al. 1999 [12]	1	1	0	0	11	0	0	0	Poor	YES
Baumann et al. 2007 [13]	1	1	1	0	11	1	0	1	Fair	
Bertalanffy et al. 2002 [14]	1	1	0	0	11	0	0	0	Poor	YES
Bhardwaj et al. 2009 [15]	1	1	1	0	11	1	0	1	Good	
Bicalho et al. 2017 [16]	1	1	1	1	1	0	1	1	Fair	
Bradac et al. 2020 [17]	1	1	1	1	1	1	0	1	Good	

Brinjikji et al. 2017 [18]	1	1	1	0	11	1	0	0	Poor	YES
Bruneau et al. 2006 [19]	1	1	1	0	1	0	0	1	Fair	YES
Byun et al. 2018 [20]	1	1	1	0	11	1	0	1	Good	
Cantu et al. 2005 [21]	1	1	1	0	11	1	0	1	Good	
Cenzato et al. 2008 [22]	1	1	1	0	11	1	0	1	Good	
Chang et al. 2011 [23]	1	1	1	0	11	1	0	1	Good	
Chang et al. 1998 [24]	1	1	0	0	11	1	0	1	Good	
Chen et al. 2011 [25]	1	1	1	0	1	1	0	1	Fair	
Chen et al. 2014 [26]	1	1	1	0	1	1	0	1	Good	
Chotai et al. 2013 [27]	1	1	1	0	11	1	0	1	Good	
Consiglieri et al. 2013 [28]	1	1	1	0	1	1	0	0	Fair	YES
Clatterbuck et al. 2000 [29]	1	1	1	1	11	1	0	0	Fair	
Consales et al. 2009 [30]	1	1	1	0	1	0	1	1	Good	
Cornelius et al. 2016 [31]	1	1	1	1	1	0	0	0	Poor	YES
D'Angelo et al. 2006 [32]	1	1	1	0	11	1	0	1	Good	
Dammann et al. 2016 [33]	1	1	1	0	11	1	1	1	Good	
Dammann et al. 2017 [34]	1	1	1	0	11	1	1	1	Good	
de Oliveira et al. 2010 [35]	1	1	1	0	11	1	1	1	Good	
del Curling et al. 1991 [36]	1	1	1	0	11	0	0	0	Fair	YES

Dukatz et al. 2011 [37]	1	1	1	1	11	1	0	1	Good	
Eichberg et al. 2019 [38]	1	1	1	0	11	1	0	1	Good	
Ferroli et al. 2005 [39]	1	1	1	0	11	1	1	1	Good	
Flemming et al. 2019 [40]	1	1	1	0	11	1	0	1	Good	
Flemming et al. 2012 [41]	1	1	1	0	11	1	0	1	Good	
Fritschi et al. 1994 [42]	1	1	0	0	11	0	0	0	Fair	YES
Frischer et al. 2008 [43]	1	1	1	1	11	0	0	0	Poor	YES
Frischer et al. 2014 (1&2) [44]	1	1	1	1	11	1	1	1	Good	
Garcia et al. 2015 [45]	1	1	1	0	11	1	0	1	Good	
Gross et al. 2016 [46]	1	1	1	0	11	1	0	1	Good	
Gui et al. 2019 [47]	1	1	1	0	1	1	1	1	Good	
Hasegawa et al. 2002 [48]	1	1	0	0	11	1	0	1	Good	
Hauck et al. 2009 [49]	1	1	0	0	1	1	0	1	Fair	
He et al. 2017 [50]	1	1	1	0	1	1	1	1	Good	
Huang et al. 2010 [51]	1	1	0	0	11	1	0	1	Good	
Huang et al. 2006 [52]	1	1	0	0	11	0	0	1	Fair	YES
Jacobs et al. 2018 [53]	1	1	0	0	11	1	0	1	Good	
Jeon et al. 2014 [54]	1	1	1	0	11	1	0	1	Good	
Josephson et al. 2011 [55]	1	1	0	1	1	0	0	1	Fair	YES
Kalani et al. 2013 [56]	1	1	1	1	0	0	0	0	Poor	YES

Kapadia et al. 2020 [57]	1	1	0	1	1	0	0	1	Fair	YES
Karlsson et al. 1998 [58]	1	1	0	0	1	1	0	1	Fair	YES
Kearns et al. 2019 [59]	1	1	1	0	11	1	0	1	Fair	
Kefeli et al. 2019 [60]	1	1	1	1	11	0	1	1	Good	
Kida, Y. 2009 [61]	1	1	0	0	11	1	0	1	Good	
Kida et al. 2015 [62]	1	1	1	0	11	1	0	1	Good	
Kim et al. 2014 [63]	1	1	1	0	1	1	0	1	Good	
Kim et al. 1997 [64]	1	1	1	0	11	1	0	1	Good	
Kim et al. 2002 [65]	1	1	1	0	11	1	0	1	Good	
Kim et al. 2005 [66]	1	1	1	0	11	1	0	1	Good	
Kivelev et al. 2011 [67]	1	1	0	0	1	0	0	1	Fair	YES
Kondziolka et al. 2007 [68]	1	1	0	0	1	1	0	1	Fair	YES
Kondziolka et al. 1995 [69]	1	1	1	1	1	1	0	1	Fair	
Kumar et al. 2019 [70]	0	1	0	1	1	0	0	1	Fair	YES
Kupersmith et al. 2001 [71]	1	1	0	0	11	1	0	1	Good	
Kwon et al. 2013 [72]	1	1	0	1	11	0	0	1	Fair	
Labauge et al. 2000 [73]	1	1	1	1	1	1	0	1	Good	
Labauge et al. 2001 [74]	1	1	1	0	11	1	0	1	Good	
Lashkarivand et al. 2020 [75]	1	1	1	1	1	1	0	1	Fair	
Lee et al. 2012 [76]	1	1	1	0	11	1	0	1	Good	

Lee et al. 2019 [77]	1	1	1	0	11	1	0	1	Good	
Lee et al. 2008 [78]	1	1	1	0	11	1	1	1	Good	
Lee et al. 2014 [79]	1	1	0	0	11	1	0	1	Fair	
Lévêque et al. 2013 [80]	1	1	0	0	0	0	0	0	Poor	YES
Li et al. 2014 [81]	1	1	1	1	11	0	1	1	Good	
Li et al. 2013 [82]	1	1	1	1	11	1	0	1	Fair	
Li et al. 2018 [83]	1	1	1	1	11	1	0	1	Good	
Li et al. 2020 [84]	1	1	1	1	11	1	0	1	Good	
Li et al. 2013* [85]	1	1	1	0	11	1	0	1	Good	
Liscak et al. 2013 [86]	1	1	0	0	11	1	0	1	Good	
Liu et al. 2016 [87]	1	1	1	0	11	1	1	1	Good	
Liu et al. 2005 [88]	1	1	1	0	1	1	0	1	Good	
Lopez-Serrano et al. 2017 [89]	1	1	1	1	11	1	0	1	Good	
Lunsford et al. 2010 [90]	1	1	0	1	11	0	1	1	Good	
Maesawa et al. 1999 [91]	1	1	0	0	11	0	0	1	Fair	YES
Mai et al. 2013 [92]	1	1	1	0	11	1	0	1	Fair	
Mathiesen et al. 2003 [93]	1	1	0	0	0	0	0	1	Poor	YES
Mehdorn et al. 1998 [94]	1	1	0	0	1	0	0	1	Fair	YES
Menon et al. 2011 [95]	1	1	0	0	11	0	0	1	Fair	YES
Menzler et al. 2010 [96]	1	1	1	1	11	0	0	0	Poor	YES
Monaco et al. 2010 [97]	1	1	0	0	11	0	0	1	Fair	YES
Moore et al. 2014 [98]	1	1	1	0	1	0	0	0	Fair	YES
Moriarity et al. 1999 [99]	1	1	0	0	11	0	0	1	Fair	YES

Mottolese et al. 2001 [100]	1	1	0	0	1	1	0	0	Fair	YES
Moultrie et al. 2014 (1&2) [101]	1	1	0	1	1	0	1	1	Good	
Nagy et al. 2019 [102]	1	1	1	0	1	0	1	1	Good	
Nagy et al. 2019 [103]	1	1	1	0	11	0	1	1	Good	
Nagy et al. 2013 [104]	1	1	1	0	1	0	0	1	Fair	YES
Nathal et al. 2018 [105]	1	1	1	0	11	1	0	1	Good	
Nikoubashman et al. 2015 [106]	1	1	1	1	11	1	0	1	Good	
Noh et al. 2014 [107]	1	1	1	0	1	0	0	1	Fair	YES
Ojemann et al. 1999 [108]	1	1	0	0	0	0	0	0	Poor	YES
Ohue et al. 2010 [109]	1	1	1	0	11	0	0	0	Fair	YES
Pandey et al. 2013 [110]	1	1	1	0	11	1	0	1	Good	
Park et al. 2018 [111]	1	1	1	0	11	1	1	1	Good	
Porter et al. 1997 [112]	1	1	0	0	11	0	0	0	Fair	YES
Porter et al. 1999 [113]	1	1	0	0	11	1	0	1	Fair	
Ramina et al. 2013 [114]	1	0	0	0	0	0	0	0	Poor	YES
Rangel-Castilla et al. 2015 [115]	1	1	0	1	11	1	0	1	Good	
Regis et al. 2000 [116]	1	1	0	0	11	1	0	1	Fair	
Ren et al. 2017 [117]	1	1	0	0	11	0	0	1	Fair	YES
Robinson et al. 1991 [118]	1	1	0	1	11	1	0	1	Good	

Sager et al. 2014 [119]	1	1	1	0	1	1	0	1	Good	
Samii et al. 2001 [120]	1	1	1	0	11	1	0	1	Good	
Sawarkar et al. 2017 [121]	1	1	1	0	11	1	0	1	Good	
Schneble et al. 2012 [122]	1	1	1	1	1	1	0	1	Good	
Schwartz et al. 2013 [123]	1	1	1	0	11	1	0	1	Good	
Sheen et al. 2018 [124]	1	1	0	0	11	0	0	1	Fair	YES
Shih et al. 2005 [125]	1	1	0	0	1	1	0	1	Fair	YES
Tian et al. 2017 [126]	1	1	1	0	11	1	0	1	Good	
Tsuji et al. 2019 [127]	1	1	1	0	11	1	0	1	Good	
Vale et al. 2015 [128]	1	1	1	1	11	1	0	1	Good	
Wang et al. 2018 [129]	1	1	1	1	11	1	0	1	Good	
Wang et al. 2003 [130]	1	1	1	0	1	0	0	1	Fair	YES
Wang et al. 2015 [131]	1	1	1	0	1	1	0	1	Good	
Winkler et al. 2006 [132]	1	1	1	0	11	0	0	0	Poor	YES
Wostrack et al. 2012 [133]	1	1	1	0	11	1	0	1	Good	
Woydt et al. 2001 [134]	1	1	1	0	11	1	0	1	Fair	
Wu et al. 2015 [135]	1	1	1	0	11	1	0	1	Good	
Yang et al. 2018 [136]	1	1	1	0	11	1	1	1	Good	
Yoon et al. 1998 [137]	1	1	1	0	1	1	0	1	Good	

Zabramski et al. 2014 [138]	1	1	1	1	11	1	0	1	Good	
Zaidi et al. 2014 [139]	1	1	1	0	11	1	0	1	Good	
Zaidi et al. 2017 [140]	1	1	0	0	11	0	0	1	Fair	YES
Zanello et al. 2019 [141]	1	1	0	1	1	0	0	0	Fair	YES
Zhang et al. 2016 [142]	1	1	1	1	11	1	1	1	Good	
Zhao et al. 2007 [143]	1	1	1	0	11	1	0	0	Good	
Zheng et al. 2020 [144]	1	1	1	1	11	1	0	1	Good	
Zuurbier et al. 2019 [145]	1	1	1	1	11	1	1	1	Good	
Zimmerman et al. 1991 [146]	1	1	0	0	11	1	0	0	Fair	YES

Table 2: The final evaluation of the risk of bias using the Newcastle-Ottawa Scale. Note: the exclusion was based on two factors: (1) NOS score ≤5*, or/and (2) less than 2* within the evaluation of study's outcomes.

eMethods 4. Data extraction

Data extraction—overview
Study design
prospective, retrospective
Patient demographics
age of patients (mean, median, SD)
number of males/females
number of paediatric/adult patients
CCM characteristics
number of CCMs
sporadic/familiar form (1—present, 0—not present/unavailable data)
mean, median, SD lesion size (in cm/cm3)
incidental/symptomatic findings (1—present, 0—not present/unavailable data)
number of patients with lobar, deep-seated, brainstem, cerebellar CCM(s)
Treatment
Observation:
number of patients with haemorrhage before/after initial identification
number of haemorrhages before/after initial identification
mean, median time of bleeding (months)
patients who bled (%)
results of haemorrhages

Surgery:
number of patients with haemorrhage – preoperatively and postoperatively
number of patients with neurodeficits – preoperatively and postoperatively
number of patients with seizures – preoperatively and postoperatively
Radiosurgery:
number of patients with haemorrhage – preoperatively and postoperatively
number of patients with neurodeficits – preoperatively and postoperatively
number of patients with seizures – preoperatively and postoperatively
mean, median marginal dose (in Gy)
SRS modality (Gamma Knife (GK), Linear Accelerator (LINAC) etc.)
Outcomes
morbidity (%)
mortality (%)
the length of follow-up (mean, median and SD in months)

Table 3: The type of extracted data. Used abbreviations: CCM, cerebral cavernous malformation; GK, gamma knife; GOS, Glasgow Outcome Scale; Gy, gray; KPS, Karnofsky Performance Scale; LINAC, linear accelerator; SD, standard deviation.

eFigure 5. The cumulative incidence – tables and forest plots

Natural history

Authors	N	Mortality/morbidity, %	Efficacy, %
Al-Holou et al. 2012 [5]	56	8.93	89.29
Al-Shahi Salman et al. 2012 [6]	134	28.36	95.60
Arauz et al. 2017 [10]	62	27.20	67.70
Bicalho et al. 2017 [16]	49	NA	83.70
Clatterbuck et al. 2000 [29]	68	26.40	86.77
Dammann et al. 2016 [33]	199	6.50	78.40
Flemming et al. 2019 [147]	51	15.70	72.60
Flemming et al. 2012 [41]	292	38.01	89.04
Gross et al. 2016 [46]	167	29.00	85.00
Jeon et al. 2014 [54]	326	23.93	87.10
Kearns et al. 2019 [59]	84	32.14	67.86
Kim et al. 1997 [64]	62	54.84	96.80
Kondziolka et al. 1995 [69]	122	15.57	93.40
Kupersmith et al. 2001 [71]	37	8.10	16.30
Labauge et al. 2000 [73]	40	17.50	65.00
Labauge et al. 2001 [74]	33	3.03	90.90
Li et al. 2014 [81]	331	29.40	60.40
Li et al. 2020 [84]	708	30.30	76.00
Moultrie et al. 2014 (1) [101]	109	27.03	84.00
Robinson et al. 1991 [118]	66	21.96	87.70
Schneble et al. 2012 [122]	87	NA	90.00

Tian et al. 2017 [126]	121	47.95	57.65
Zabramski et al. 2014 [138]	21	14.28	66.70
Zheng et al. 2020 [144]	48	16.68	77.10
Zuurbier et al. 2019 [145]	300	14.00	86.00

Table 4: The overview of conservative treatment series. Used abbreviations: NA, not applicable.

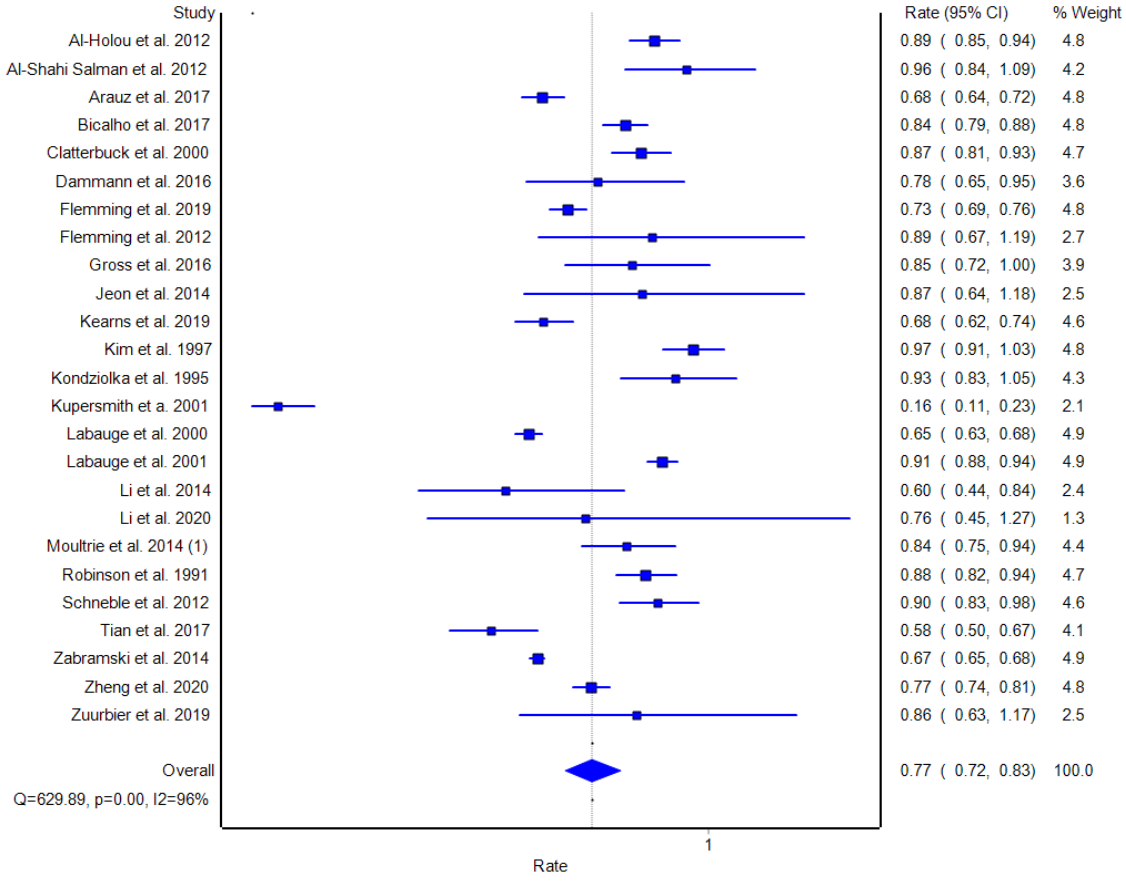

Figure 2: The efficacy of conservative treatment.

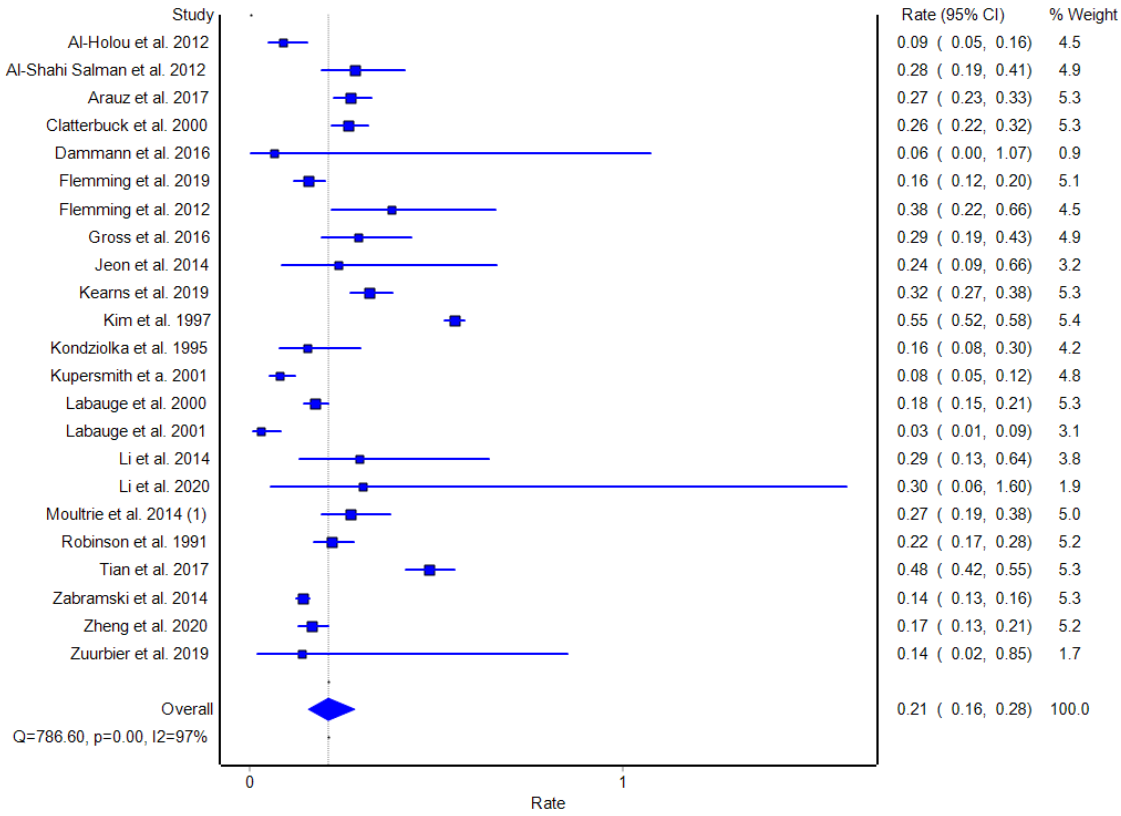

Figure 3: The morbidity/mortality rate from conservative treatment. Two studies [16, 122] must have been excluded due to unavailable data.

Surgery

Authors	N	Mortality/morbidity, %	Efficacy, %
Abla et al. 2011 [1]	260	40.40	93.00
Acciari et al. 2009 [2]	42	7.14	100.00
Amato et al. 2013 [7]	26	7.69	100.00
Amin-Hanjani et al. 1998 [9]	94	6.20	98.00
Arauz et al. 2017 (1) [10]	37	10.20	100.00
Baumann et al. 2007 [13]	168	9.00	100.00
Bradac et al. 2020 [17]	58	11.90	96.00
Byun et al. 2018 [20]	47	27.60	91.00
Cenzato et al. 2008 [22]	30	3.30	97.00
Chang et al. 2011 [23]	79	8.86	100.00
Chen et al. 2011 [25]	55	14.50	100.00
Chen et al. 2014 [26]	38	10.52	100.00
Chotai et al. 2013 [27]	59	14.70	98.00
Consales et al. 2009 [30]	32	7.10	97.00
D'Angelo et al. 2006 [32]	118	7.00	98.00
Dammann et al. 2017 [34]	79	3.00	100.00
de Oliviera et al. 2010 [35]	45	11.10	100.00
Dukatz et al. 2011 [37]	71	11.00	100.00
Eichberg et al. 2019 [38]	20	5.00	100.00
Ferroli et al. 2005 [39]	52	20.90	100.00
Frischer et al. 2014 (1) [44]	29	25.00	62.00
Garcia et al. 2015 [45]	104	10.56	95.00

Gui et al. 2019 [47]	67	5.97	100.00
Hauck et al. 2009 [49]	44	11.00	95.00
He et al. 2017 [50]	181	5.00	100.00
Huang et al. 2010 [51]	22	13.90	95.00
Kwon et al. 2013 [72]	56	16.70	100.00
Lashkarivand et al. 2020 [75]	22	4.50	100.00
Lee et al. 2008 [78]	25	10.10	100.00
Li et al. 2013 [82]	242	12.36	97.00
Li et al. 2018 [83]	27	18.20	96.00
Li et al. 2013* [85]	47	18.20	98.00
Mai et al. 2013 [92]	22	14.00	90.00
Moultrie et al. 2014 (2) [101]	25	10.00	96.00
Nathal et al. 2018 [105]	50	22.00	92.00
Pandey et al. 2013 [110]	176	15.90	97.00
Porter et al. 1999 [113]	100	10.00	100.00
Rangel-Castilla et al. 2015 [115]	46	9.00	100.00
Samii et al. 2001 [120]	36	13.80	100.00
Sawarkar et al. 2017 [121]	50	12.80	100.00
Schwartz et al. 2013 [123]	35	9.10	94.00
Tsuji et al. 2019 [127]	72	7.10	98.00
Vale et al. 2015 [128]	34	3.00	100.00
Wang et al. 2018 [129]	23	0.23	100.00
Wang et al. 2015 [131]	23	4.30	95.00

Wostrack et al. 2012 [133]	45	4.00	100.00
Woydt et al. 2001 [134]	35	13.00	97.00
Wu et al. 2015 [135]	58	3.40	100.00
Yang et al. 2018 [136]	47	14.80	100.00
Zaidi et al. 2014 [139]	31	3.20	96.00
Zhang et al. 2016 [142]	120	11.10	98.00
Zhao et al. 2007 [143]	70	8.60	100.00

Table 5: The overview of surgical series.

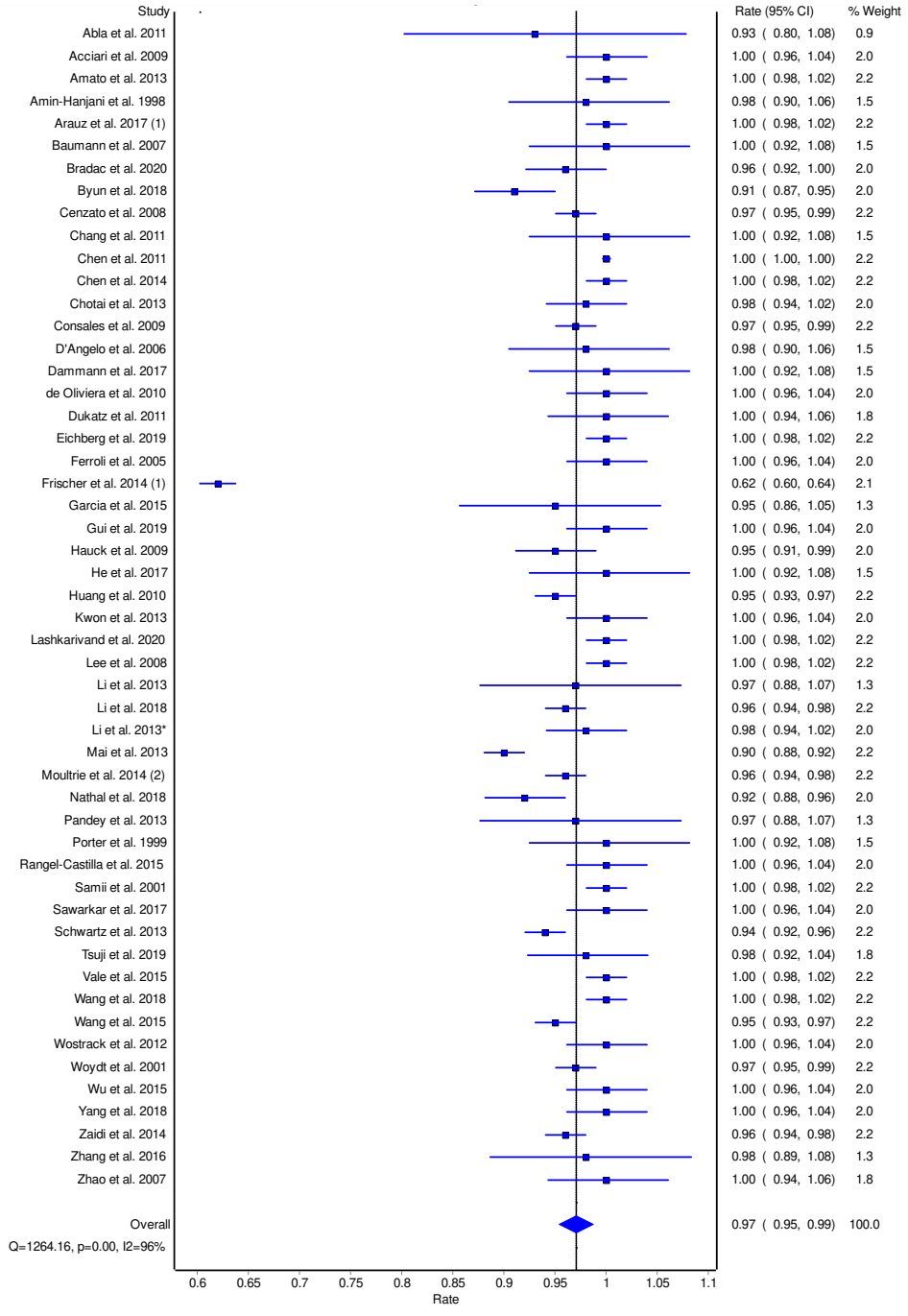

Figure 4: Surgical efficacy.

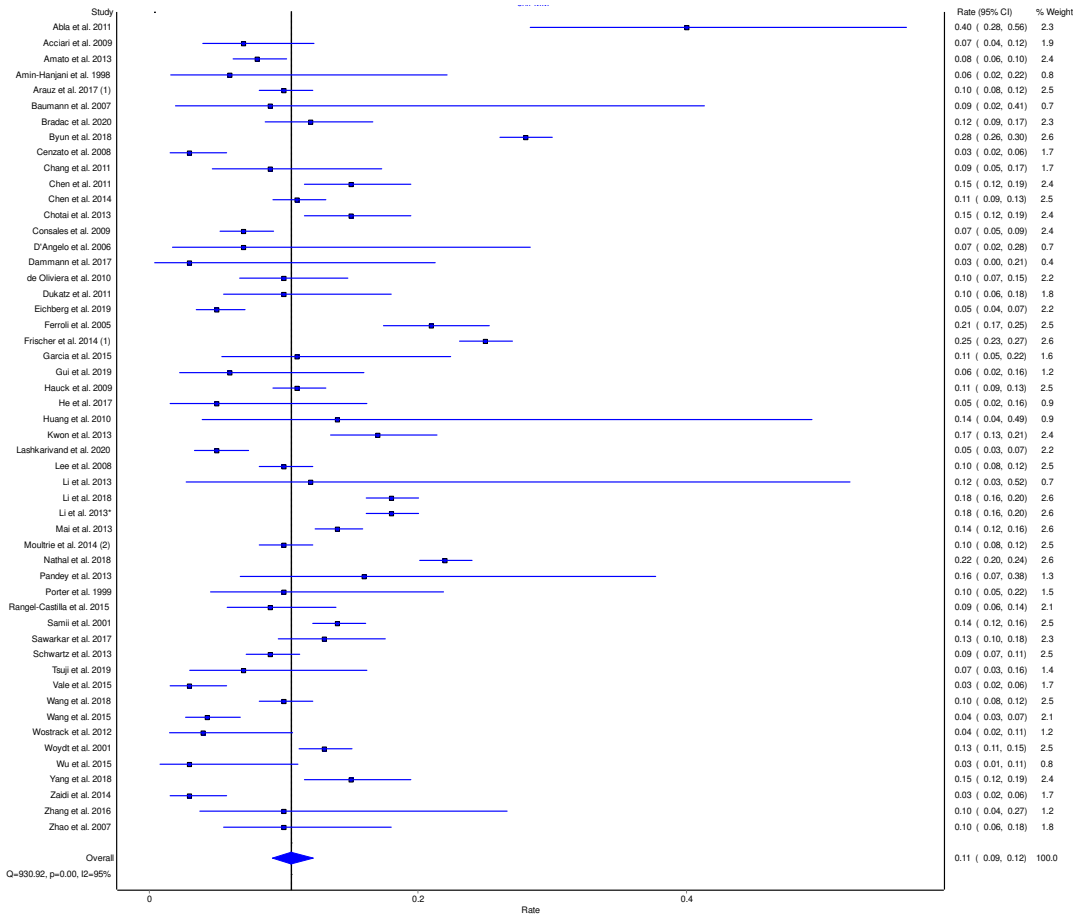

Figure 5: Surgical morbidity/mortality rate.

Radiosurgery

Authors	N	Mortality/morbidity, %	Efficacy, %
Chang et al. 1998 [24]	57	17.50	68.42
Frischer et al. 2014 (2) [44]	38	7.80	84.21
Hasegawa et al. 2002 [48]	82	7.32	81.71
Jacobs et al. 2018 [53]	76	20.00	80.26
Kefeli et al. 2019 [60]	82	3.00	96.34
Kida et al. 2015 [62]	298	7.12	79.53
Kim et al. 2014 [63]	39	10.30	84.61
Kim et al. 2002 [65]	22	9.00	95.45
Kim et al. 2005 [66]	42	7.10	97.61
Lee et al. 2012 [148]	49	4.10	87.76
Lee et al. 2019 [77]	261	3.50	80.08
Lee et al. 2014 [79]	49	2.00	100.00
Liscak et al. 2013 [86]	112	10.04	90.18
Liu et al. 2016 [87]	43	11.60	90.70
Liu et al. 2005 [88]	125	17.85	74.40
Lopez-Serrano et al. 2017 [89]	95	14.70	94.74
Lunsford et al. 2010 [90]	103	13.50	74.76
Nagy et al. 2019 (1) [102]	210	8.39	87.14
Nagy et al. 2019 (2) [103]	96	8.95	91.67
Park et al. 2018 [111]	45	2.60	77.78

Regis et al. 2000 [116]	49	10.20	97.96
Sager et al. 2014 [119]	52	14.90	94.23
Yoon et al. 1998 [137]	22	18.00	72.72

Table 6: The overview of radiosurgical series.

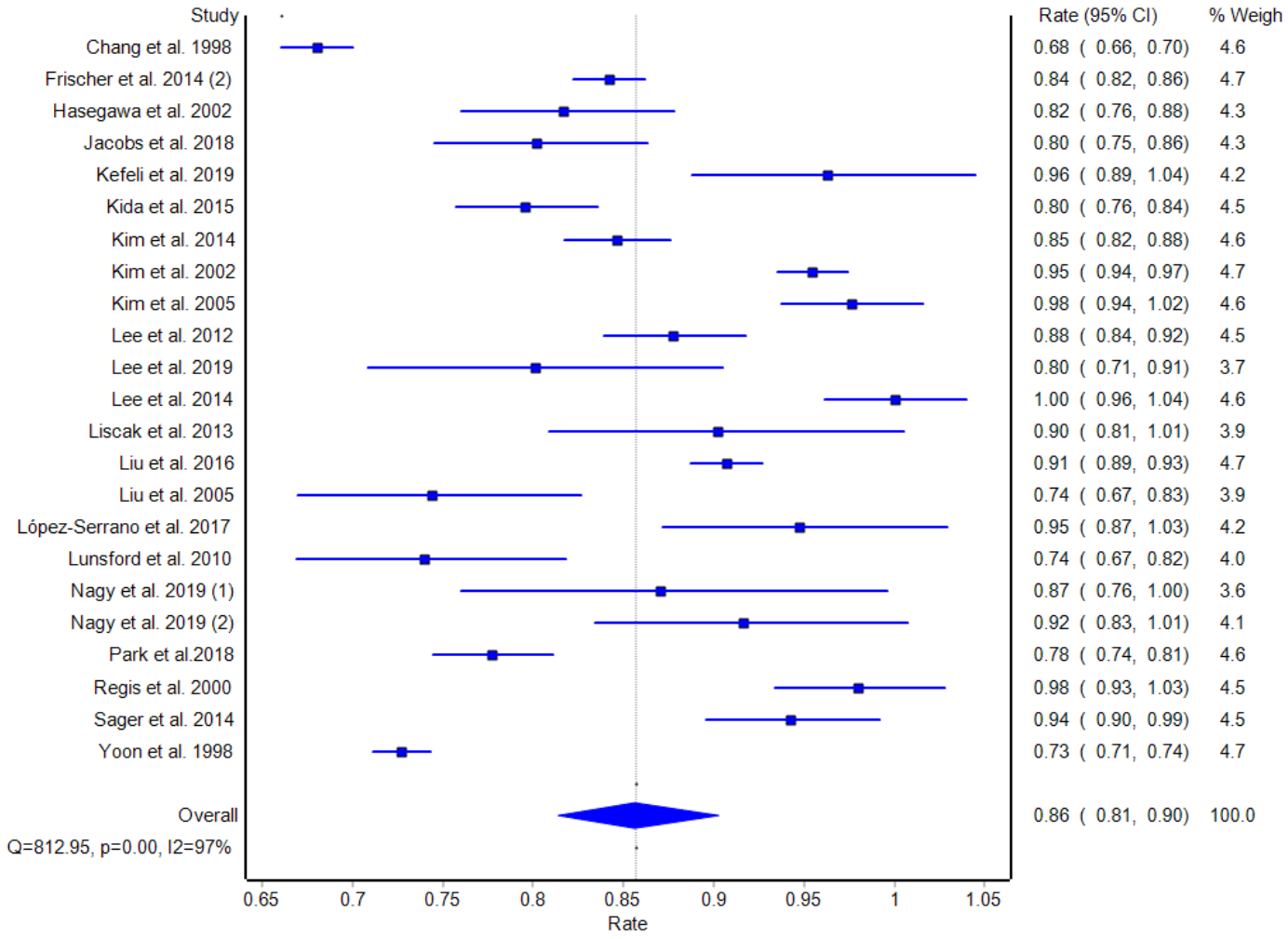

Figure 6: Radiosurgical efficacy.

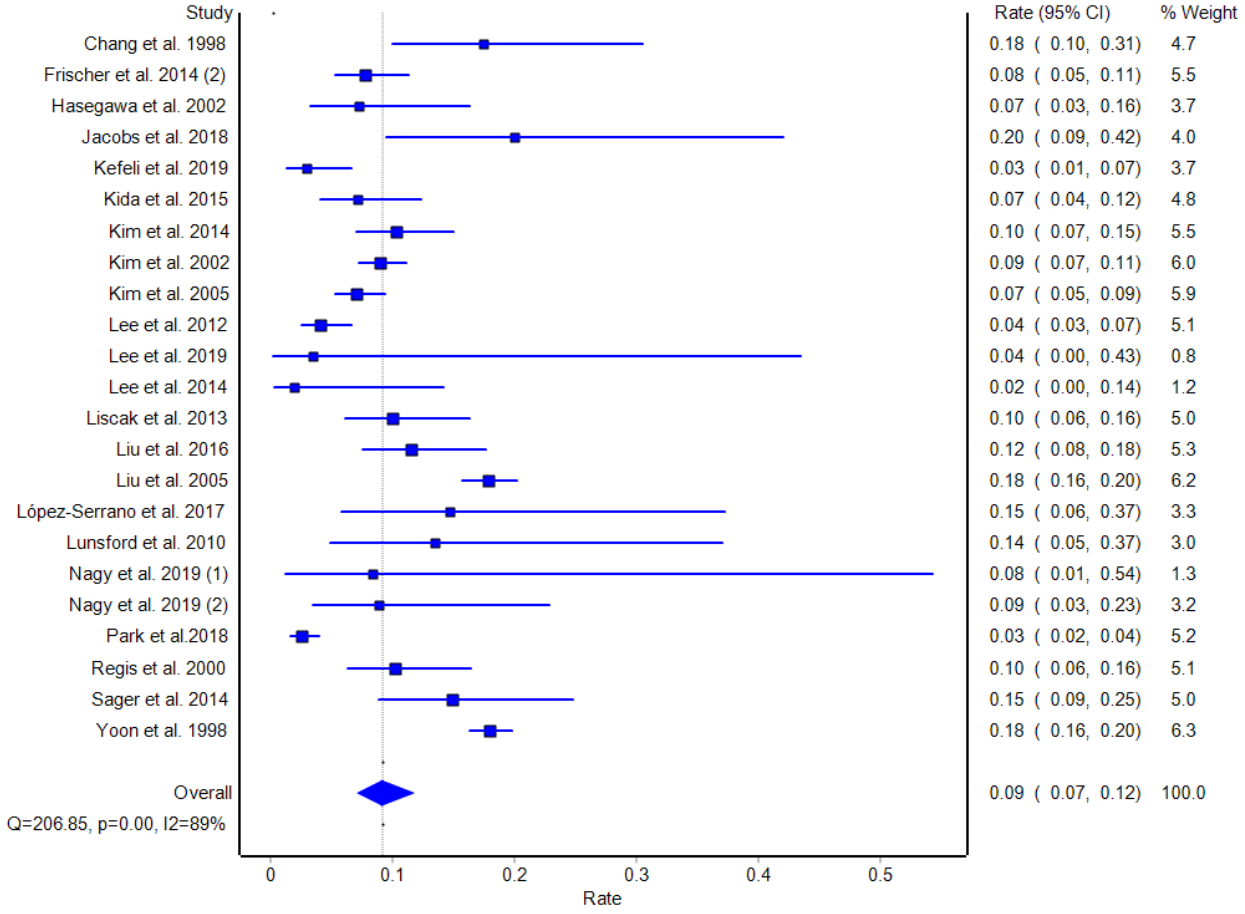

Figure 7: Radiosurgical morbidity/mortality rate.

eTable 6. Sensitivity analysis – evaluation of haemorrhage rate in high-quality cohorts

Sensitivity analysis (n = 37)			
	RR	**95% CI**	**p-value**
Males	0.970	0.950–0.980	<.001
Initial ICH	1.005	1.002–1.008	.002
CCM			
Lobar	0.997	0.995–0.997	.088
Deep	1.005	1.001–1.008	.008
Brainstem	1.006	1.004–1.009	<.001
Cerebellum	0.977	0.961–0.9924	.004

Table 7: The sensitivity analysis of high-quality cohorts. Used abbreviations: CCM, cerebral cavernous malformation; CI, confidence interval; ICH, intracerebral haemorrhage; RR, rate ratio.

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