EUROPEAN STROKE ORGANISATION

Management of space-occupying brain infarction

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Guideline Webinar

18 – 60 years | ≤ 48 hours

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PICO 1

In patients with space-occupying hemispheric infarction aged 18 up to and including 60 years, does surgical decompression initiated within 48 hours of stroke onset as compared to no surgical decompression reduce the risk of death or poor outcome?

poor outcome = mRS 4 - 6

recommendations based on RCTs

18 – 60 years

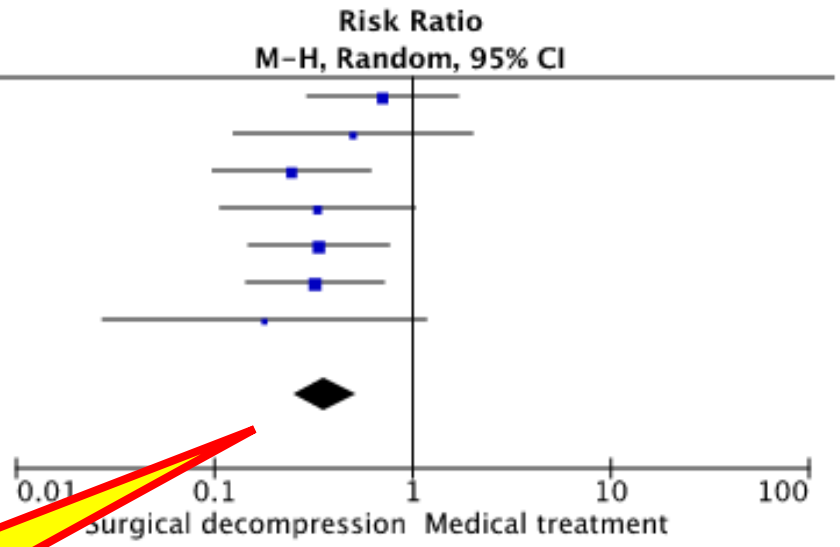
≤ 48 hours

surgical decompression – risk of death

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chua 2015, HeMMI	5	13	6	11	18.3%	0.71 [0.29, 1.69]
Frank 2014, HeADDFIRST	2	6	2	3	7.3%	0.50 [0.13, 2.00]
Hofmeijer 2009, HAMLET	4	21	14	18	16.6%	0.24 [0.10, 0.61]
Jüttler 2007, DESTINY	3	17	8	15	10.9%	0.33 [0.11, 1.03]
Kumral 2021, DEMITUR	5	23	22	34	21.1%	0.34 [0.15, 0.76]
Vahedi 2007, DECIMAL	5	20	14	18	21.9%	0.32 [0.14, 0.71]
Zhao 2012	1	8	7	10	4.0%	0.18 [0.03, 1.17]
Total (95% CI)		**108**		**109**	**100.0%**	**0.36 [0.25, 0.53]**
Total events	25		73			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.95$, df = 6 (P = 0.68); $I^2 = 0\%$

Test for overall effect: Z = 5.33 (P < 0.00001)



n = 217

ARR 44%

18 – 60 years | ≤ 48 hours

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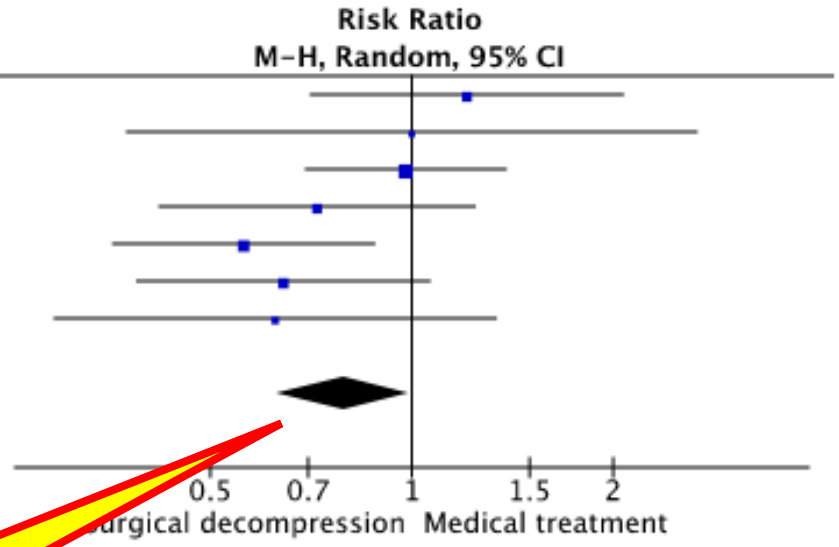
surgical decompression – risk of poor outcome

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chua 2015, HeMMI	10	13	7	11	14.0%	1.21 [0.71, 2.07]
Frank 2014, HeADDFIRST	4	6	2	3	5.0%	1.00 [0.38, 2.66]
Hofmeijer 2009, HAMLET	16	21	14	18	25.8%	0.98 [0.69, 1.38]
Jüttler 2007, DESTINY	9	17	11	15	13.8%	0.72 [0.42, 1.24]
Kumral 2021, DEMITUR	11	23	29	34	18.2%	0.56 [0.36, 0.88]
Vahedi 2007, DECIMAL	10	20	14	18	15.4%	0.64 [0.39, 1.06]
Zhao 2012	4	8	8	10	7.9%	0.63 [0.29, 1.34]
Total (95% CI)		**108**		**109**	**100.0%**	**0.79 [0.63, 0.99]**
Total events	64		85			

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 7.82$, df = 6 (P = 0.25); $I^2 = 23\%$

Test for overall effect: Z = 2.01 (P = 0.04)



ARR 19%

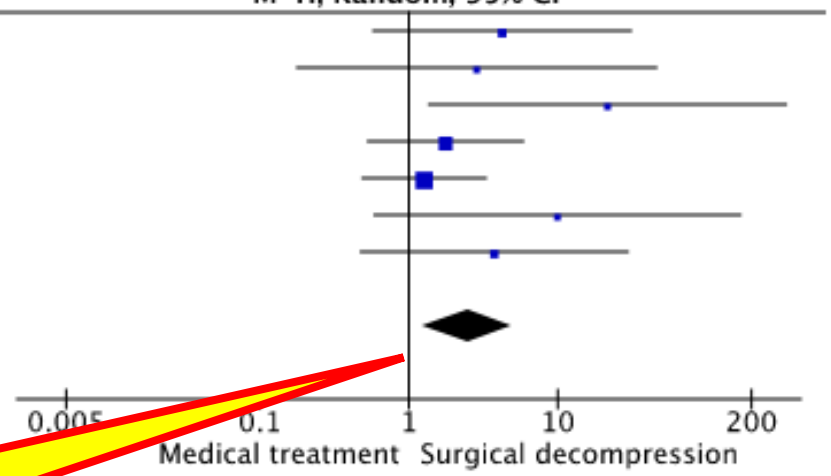
18 – 60 years | ≤ 48 hours

surgical decompression – mRS 4, 5

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Chua 2015, HeMMI	5	13	1	11	11.1%	4.23 [0.58, 30.99]
Frank 2014, HeADDFIRST	2	6	0	3	6.0%	2.86 [0.18, 45.91]
Hofmeijer 2009, HAMLET	12	21	0	18	6.1%	21.59 [1.37, 340.88]
Jüttler 2007, DESTINY	6	17	3	15	25.5%	1.76 [0.53, 5.86]
Kumral 2021, DEMITUR	6	23	7	34	35.0%	1.27 [0.49, 3.29]
Vahedi 2007, DECIMAL	5	20	0	18	5.8%	9.95 [0.59, 168.27]
Zhao 2012	3	8	1	10	10.4%	3.75 [0.48, 29.52]
Total (95% CI)		**108**		**109**	**100.0%**	**2.49 [1.23, 5.04]**
Total events	39		12			

Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 7.01$, df = 6 (P = 0.32); $I^2 = 14\%$

Test for overall effect: Z = 2.53 (P = 0.01)



absolute increase 25%

18 – 60 years | ≤ 48 hours

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evidence-based recommendation

We recommend surgical decompression to reduce the risk of death or a poor outcome.

Surgery should only be done after a shared decision process including a careful discussion with the patient or his/her representatives about the risk of survival with substantial disability.

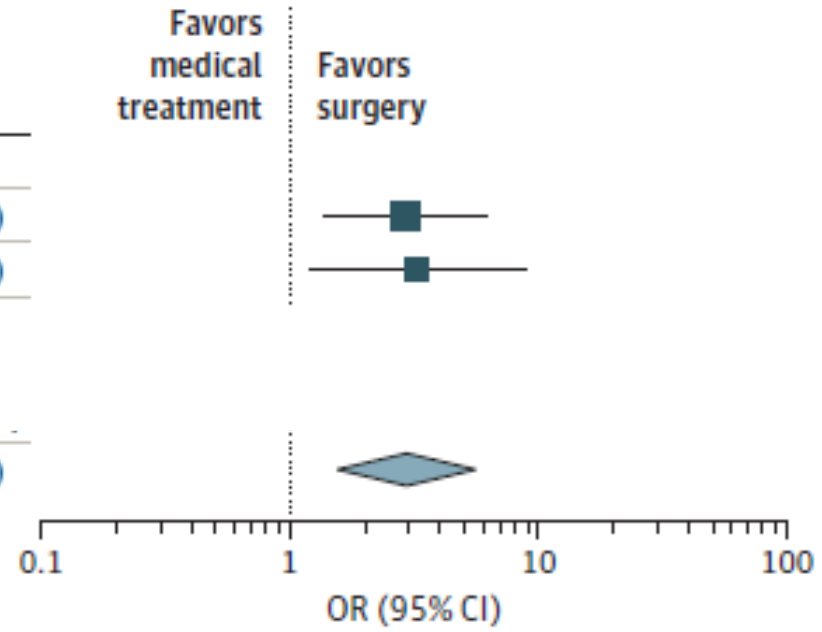
Quality of evidence: **moderate** ⊕⊕⊕

Strength of recommendation: **Strong** ↑↑

aphasia

surgical decompression – favourable outcome (mRS ≤ 3)

Characteristic	No. (%) of patients: Surgery (n = 234)	Medical (n = 254)	OR (95% CI)
Aphasia (*P* = .43)			
Absent	44/128 (34)	21/138 (15)	2.93 (1.38-6.21)
Present	43/106 (41)	16/116 (14)	3.26 (1.20-8.85)
Summary			2.95 (1.55-5.60)



Reinink 2021

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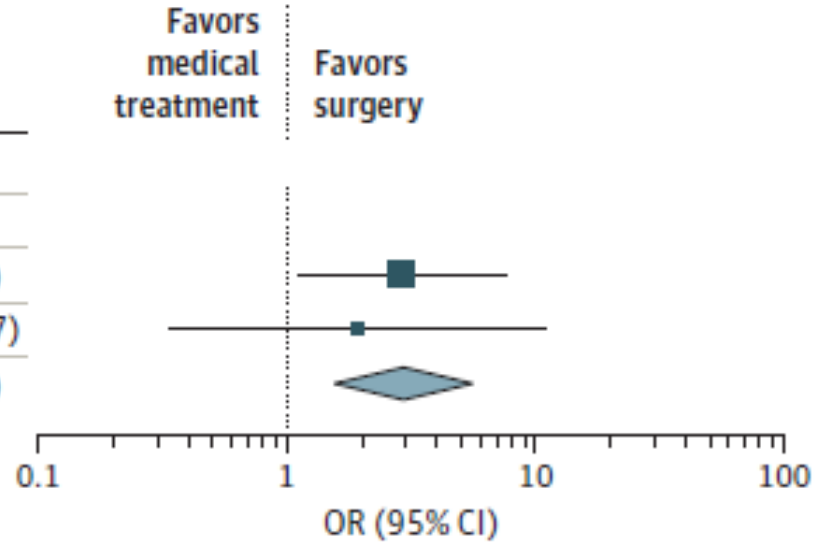
expert consensus statement

The benefit of surgical decompression does not depend on the absence or presence of aphasia.

additional vascular territory

surgical decompression – favourable outcome (mRS ≤ 3)

Characteristic	No. (%) of patients: Surgery (n = 234)	Medical (n = 254)	OR (95% CI)
Vascular territory (*P* > .99)[c]			
MCA only	27/97 (28)	15/103 (15)	2.89 (1.11-7.56)
MCA and ACA and/or PCA	30/69 (44)	14/89 (16)	1.92 (0.34-10.87)
Summary			2.95 (1.55-5.60)



Reinink 2021

additional vascular territory

expert consensus statement

The benefit of surgical decompression does not depend on the presence of an infarct in the territory of the anterior or posterior cerebral artery in addition to that of the middle cerebral artery.

18 – 60 years | > 48 hours

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PICO 2

In patients with space-occupying hemispheric infarction aged 18 up to and including 60 years, does surgical decompression initiated later than 48 hours of stroke onset as compared to no surgical decompression reduce the risk of death or poor outcome?

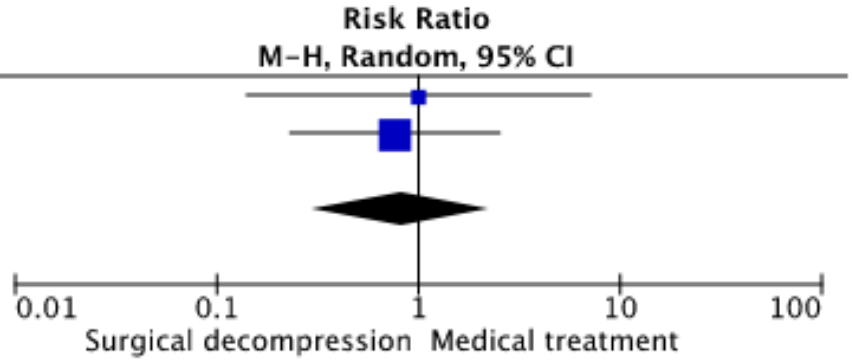
18 – 60 years | > 48 hours

surgical decompression – risk of death

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Frank 2014, HeADDFIRST	2	6	1	3	27.1%	1.00 [0.14, 7.10]
Hofmeijer 2009, HAMLET	3	11	5	14	72.9%	0.76 [0.23, 2.52]
Total (95% CI)		**17**		**17**	**100.0%**	**0.82 [0.30, 2.28]**
Total events	5		6			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.05$, df = 1 (P = 0.82); $I^2 = 0\%$
Test for overall effect: Z = 0.38 (P = 0.71)

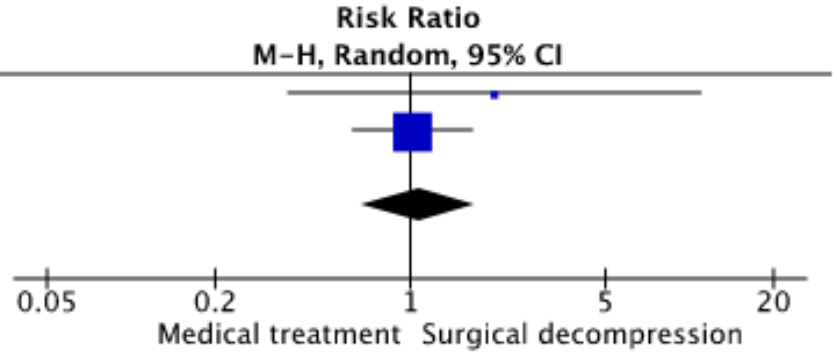
n = 34



surgical decompression – risk of poor outcome

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Frank 2014, HeADDFIRST	4	6	1	3	7.7%	2.00 [0.37, 10.92]
Hofmeijer 2009, HAMLET	8	11	10	14	92.3%	1.02 [0.62, 1.66]
Total (95% CI)		**17**		**17**	**100.0%**	**1.07 [0.67, 1.72]**
Total events	12		11			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.64$, df = 1 (P = 0.42); $I^2 = 0\%$
Test for overall effect: Z = 0.29 (P = 0.77)



18 – 60 years | > 48 hours

evidence-based recommendation

There is continued uncertainty about the benefit and risks of the use of surgical decompression as a means to reduce the risk of death or a poor outcome.

Quality of evidence: **low** ⨁⨁

Strength of recommendation: -

18 – 60 years | > 48 hours

expert consensus statement

Surgical decompression should also be considered later than 48 hours after stroke onset if based on clinical grounds death due to herniation appears likely.

≥ 61 years | ≤ 48 hours

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PICO 3

In patients with space-occupying hemispheric infarction aged 61 years or older, does surgical decompression initiated within 48 hours of stroke onset as compared to no surgical decompression reduce the risk of death or poor outcome?

≥ 61 years

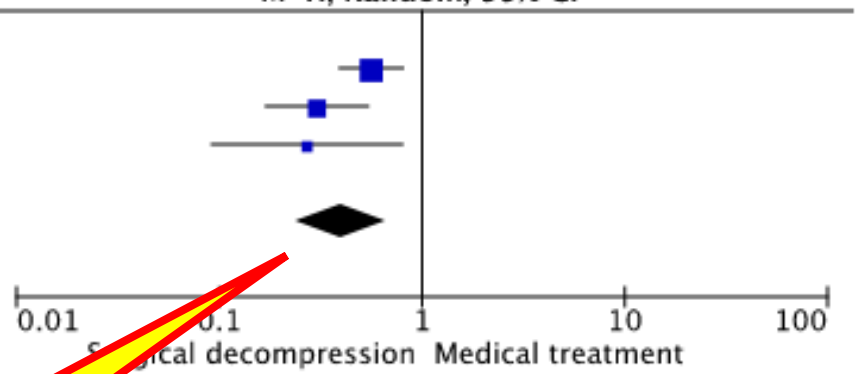
≤ 48 hours

surgical decompression – risk of death

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Frank 2014, HeADDFIRST	0	0	0	1		Not estimable
Jüttler 2014, DESTINY II	20	47	47	62	48.5%	0.56 [0.39, 0.81]
Kumral 2021, DEMITUR	10	47	33	47	35.0%	0.30 [0.17, 0.54]
Zhao 2012	3	16	9	13	16.5%	0.27 [0.09, 0.80]
Total (95% CI)		**110**		**123**	**100.0%**	**0.40 [0.24, 0.67]**
Total events	33		89			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 4.26$, df = 2 (P = 0.12); $I^2 = 53\%$

Test for overall effect: Z = 3.51 (P = 0.0005)



n = 232

ARR 42%

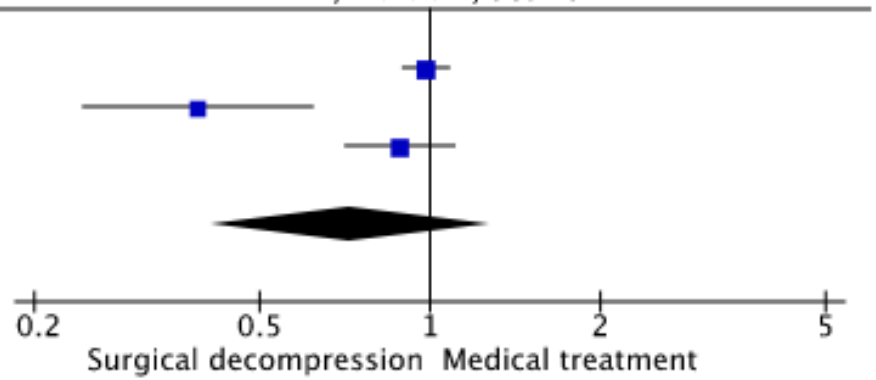
≥ 61 years | ≤ 48 hours

surgical decompression – risk of poor outcome

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Frank 2014, HeADDFIRST	0	0	1	1		Not estimable
Jüttler 2014, DESTINY II	44	47	59	62	36.1%	0.98 [0.90, 1.08]
Kumral 2021, DEMITUR	14	47	36	47	29.3%	0.39 [0.24, 0.62]
Zhao 2012	14	16	13	13	34.6%	0.88 [0.71, 1.10]
Total (95% CI)		**110**		**123**	**100.0%**	**0.72 [0.41, 1.28]**
Total events	72		109			

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 39.44$, df = 2 ($P < 0.00001$); $I^2 = 95\%$

Test for overall effect: Z = 1.12 (P = 0.26)



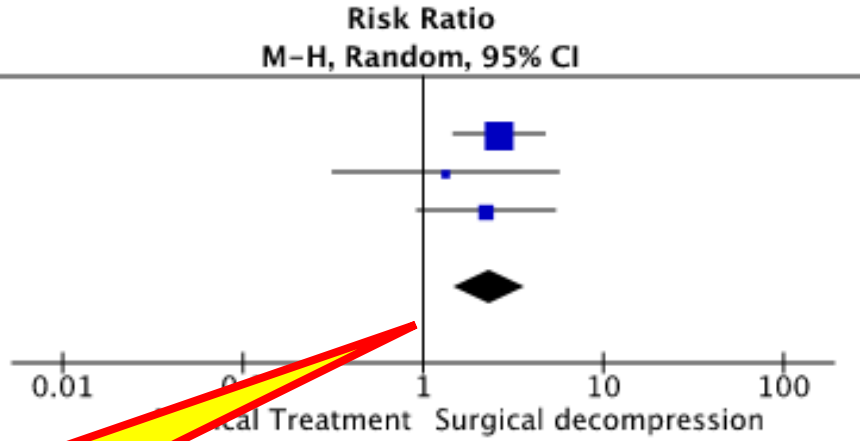
≥ 61 years | ≤ 48 hours

surgical decompression – risk of mRS 4, 5

Study or Subgroup	Surgical decompression Events	Total	Medical treatment Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Frank 2014, HeADDFIRST	0	0	1	1		Not estimable
Jüttler 2014, DESTINY II	24	47	12	62	62.6%	2.64 [1.48, 4.71]
Kumral 2021, DEMITUR	4	47	3	47	10.1%	1.33 [0.32, 5.63]
Zhao 2012	11	16	4	13	27.2%	2.23 [0.93, 5.39]
Total (95% CI)		**110**		**122**	**100.0%**	**2.35 [1.49, 3.72]**
Total events	39		19			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.76$, df = 2 (P = 0.68); $I^2 = 0\%$

Test for overall effect: Z = 3.65 (P = 0.0003)



absolute increase 19%

≥ 61 years | ≤ 48 hours

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evidence-based recommendation

We suggest considering surgical decompression to reduce the risk of death.

Surgery should only be done after a shared decision process including a careful discussion with the patient or his/her representatives about the risk of survival with substantial disability.

Quality of evidence: **low** ⨁⨁

Strength of recommendation: **weak** ↑?

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PICO 4

In patients with space-occupying cerebellar infarction, does surgical decompression as compared to no surgical decompression reduce the risk of death or a poor outcome?

<u>literature search</u>

- no RCTs
- observational studies suggest better outcomes with surgery

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evidence-based recommendation

There is continued uncertainty about the benefit and risks of surgical decompression as a means to reduce the risk of death or a poor outcome.

Quality of evidence: **very low** ⊕

Strength of recommendation: **-**

infarct in cerebellum

expert consensus statement

We suggest considering surgical decompression with or without CSF drainage in selected patients with space-occupying cerebellar infarction, such as in those with a reduced consciousness caused by brainstem compression.

The precise selection of patients and the optimal timing of treatment remain uncertain. There is insufficient evidence to support its routine use.

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PICO 5

In patients with space-occupying cerebellar infarction, does CSF drainage as compared to no CSF drainage reduce the risk of death or a poor outcome?

<u>literature search</u>

- no RCTs
- no high-quality observational studies

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evidence-based recommendation

There is continued uncertainty about the benefit and risks of CSF drainage as a means to reduce the risk of death or a poor outcome.

Quality of evidence: **very low** ⊕

Strength of recommendation: **-**

expert consensus statement

We suggest considering CSF drainage alone or combined with surgical decompression in selected patients with space-occupying cerebellar infarction and signs of an obstructive hydrocephalus, such as in those with a reduced consciousness.

The selection of patients and the optimal timing of treatment remain uncertain. There is insufficient evidence to support its routine use.

medical treatment

- osmotic therapy
- hyperventilation
- corticosteroids
- sedation

→ no RCT
no convincing evidence from other studies

- hypothermia
- glyburide

→ one inconclusive phase II RCT

expert consensus statements*

We suggest against the use of corticosteroids or glyburide in routine clinical practice

We suggest against the routine use of osmotic therapy, hyperventilation, or sedation as a means to reduce the risk of death or a poor outcome. Short-term therapy may be considered as a rescue procedure.

* summary – please see Guideline for details

PICO 12

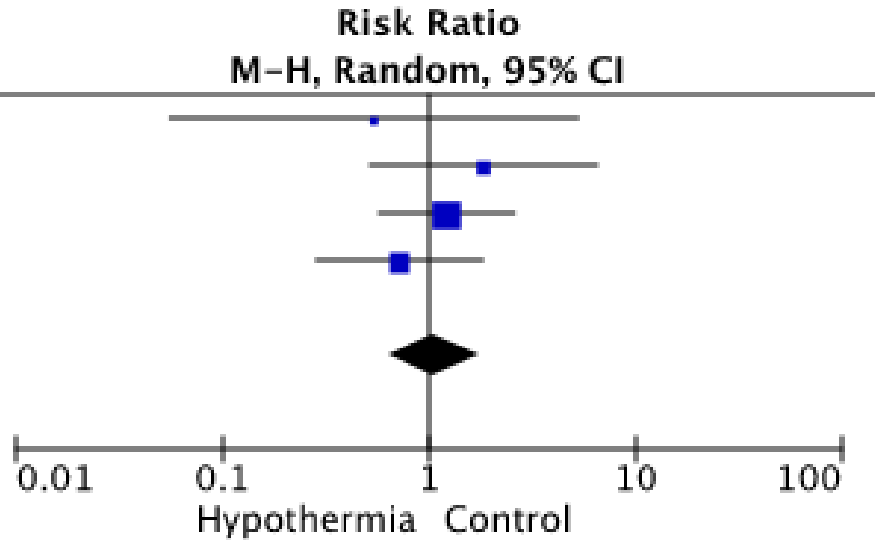
In patients with space-occupying hemispheric infarction, does hypothermia as compared to no hypothermia reduce the risk of death or a poor functional outcome?

hypothermia – risk of death

Study or Subgroup	Hypothermia Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Els 2004	1	12	2	13	5.2%	0.54 [0.06, 5.24]
Neugebauer 2019	6	25	3	23	16.6%	1.84 [0.52, 6.52]
Su 2016	8	16	7	17	47.3%	1.21 [0.57, 2.57]
Su 2018	8	25	4	9	30.9%	0.72 [0.28, 1.82]
Total (95% CI)		**78**		**62**	**100.0%**	**1.06 [0.63, 1.78]**
Total events	23		16			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.87$, df = 3 (P = 0.60); $I^2 = 0\%$

Test for overall effect: Z = 0.23 (P = 0.82)



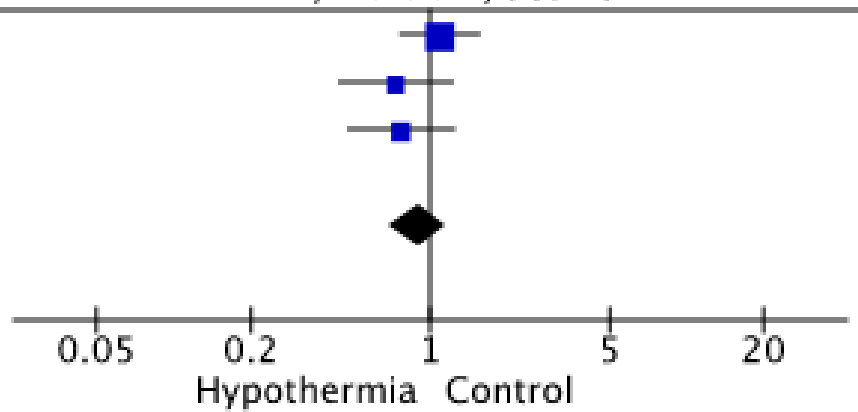
n = 140

hypothermia – risk of poor outcome

Study or Subgroup	Hypothermia Events	Hypothermia Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
Neugebauer 2019	19	25	16	23	47.8%	1.09 [0.77, 1.55]
Su 2016	9	16	13	17	24.5%	0.74 [0.44, 1.22]
Su 2018	15	25	7	9	27.7%	0.77 [0.48, 1.24]
Total (95% CI)		**66**		**49**	**100.0%**	**0.90 [0.69, 1.17]**
Total events	43		36			

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.21$, df = 2 (P = 0.33); $I^2 = 10\%$

Test for overall effect: Z = 0.79 (P = 0.43)



evidence-based recommendation

We suggest against the use of hypothermia in routine clinical practice as a means to reduce the risk of death or a poor outcome.

Quality of evidence: **very low** ⊕

Strength of recommendation: **weak ↓?**

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