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Chronic subdural hematoma: tailoring treatment

Miah, I.P.

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Supplementary appendices

Chapter 4

Table S1. Participating Hospitals

| Hospital | Number of inclusions |
|--|-----------------------------|
| Admiraal de Ruyter Hospital, Goes (referring to Erasmus Medical Center) | 4 |
| Albert Schweitzer Hospital, Dordrecht (referring to Erasmus Medical Center) | 12 |
| Erasmus Medical Center, Rotterdam | 2 |
| Groningen University Medical Center, Groningen | 8 |
| Haaglanden Medical Center, The Hague | 105 |
| Haga Hospital, The Hague | 38 |
| Isala Hospital, Zwolle | 12 |
| Leiden University Medical Center | 37 |
| Maasstad Hospital, Rotterdam (referring to Erasmus Medical Center) | 11 |
| Medisch Spectrum Twente, Enschede | 13 |
| Sint Franciscus Gasthuis and Vlietland Hospital, Rotterdam (referring to Erasmus Medical Center) | 6 |
| Van Weel Bethesda Hospital, Dirksland (referring to Erasmus Medical Center) | 4 |
| Total number of inclusions | 252 |

Table S2. Supplemental data on treatment

| Variable | Dexamethasone | Burr-hole craniostomy |
|--|---------------|-----------------------|
| Use of antithrombotic medication during surgery- no./total no. (%) | 4/71 (5.6) | 12/118 (10.2) |
| Amount of burr holes in primary surgery- no./total no. (%) | | |
| 1 burr hole | 51/71 (71.8) | 89/118 (75.4) |
| 2 burr holes | 20/71 (28.2) | 29/118 (24.6) |
| Drain placement in primary surgery- no./total no. (%) | | |
| None | 0/71 (0.0) | 1/118 (0.8) |
| Subdural drain | 55/71 (77.5) | 98/118 (83.1) |
| Subgaleal drain | 9/71 (12.7) | 13/118 (11.0) |
| Unknown which type of drain | 7/71 (9.9) | 6/118 (5.1) |
| Type of anesthesia in primary surgery- no./total no. (%) | | |
| Local | 40/70 (57.1) | 71/118 (60.2) |
| General | 30/70 (42.9) | 46/118 (39.0) |
| Unknown | 0/70 (0.0) | 1/118 (0.8) |
| Duration of dexamethasone tapering course – days | | |
| Median (min-max) | 19 (1-29) | n.a. |
| Mean ± standard deviation | 15.99 ± 5.9 | n.a. |
| IQR | 14.3-19.0 | n.a. |
| Duration between diagnosis and operation in patients randomized for dexamethasone – days | | |
| Median (min-max) | 20 (1-127) | n.a. |
| Mean ± standard deviation | 24.31 ± 21.24 | n.a. |
| IQR | | n.a. |
| Duration between diagnosis and operation in patients randomized for surgery – days | | |
| Median (min-max) | n.a. | 2 (0-127) |
| Mean ± standard deviation | n.a. | 5.16 ± 12.77 |
| IQR | n.a. | 1.0-5.0 |
| Compliance with dexamethasone tapering course – no./total no. (%) | | |
| Shorter dexamethasone course | 43/127 (33.9) | n.a. |
| Full dexamethasone course | 75/127 (59.1) | n.a. |
| Longer dexamethasone course | 6/127 (4.7) | n.a. |
| Missing | 3/127 (2.4) | n.a. |

Table S2. *continued*

| Variable | Dexamethasone | Burr-hole craniostomy |
|--|---------------|-----------------------|
| Complications up to 3 months – total no. | 136 | 66 |
| Infection (total no.) | 29/127 (22.8) | 24/125 (19.2) |
| Empyema | 2/29 (6.9) | 1/24 (4.2) |
| Gastrointestinal infection | 1/29 (3.4) | 0/24 (0.0) |
| Wound infection | 0/29 (0.0) | 1/24 (4.2) |
| Pneumonia | 8/29 (27.6) | 2/24 (8.3) |
| Sepsis | 0/29 (0.0) | 1/24 (4.2) |
| Thrombophlebitis | 0/29 (0.0) | 1/24 (4.2) |
| Urinary tract infection | 10/29 (34.5) | 9/24 (37.5) |
| Infection other | 8/29 (27.6) | 9/24 (37.5) |
| Falling | 19/127 (15.0) | 9/125 (7.2) |
| Hyperglycaemia | 25/127 (19.7) | 5/125 (4.0) |
| Delirium | 20/127 (15.7) | 7/125 (5.6) |
| Epilepsy | 16/127 (12.6) | 9/125 (7.2) |
| Insomnia | 6/127 (4.7) | 4/125 (3.2) |
| Thrombus (total no.) | 4/127 (3.1) | 3/125 (2.4) |
| Pulmonary | 3 (75.0) | 1 (33.3) |
| Other | 1 (25.0) | 2 (66.7) |
| Mood disorder | 6/127 (4.7) | 0/125 (0.0) |
| Fever | 3/127 (2.4) | 1/125 (0.8) |
| Weight gain / increased appetite | 4/127 (3.1) | 0/125 (0.0) |
| Bleeding burr-hole pathway | 2/127 (1.6) | 2/125 (1.6) |
| Wound leakage | 1/127 (0.8) | 2/125 (1.6) |
| Gastrointestinal bleeding | 1/127 (0.8) | 0/125 (0.0) |

Table S3. Supplemental table at three months – AS TREATED

| Variable | Dexamethasone only | Dexamethasone, additional burr-hole craniostomy | Burr-hole craniostomy only | Burr-hole craniostomy, additional dexamethasone | No treatment |
|---|--------------------|---|----------------------------|---|----------------|
| modified Rankin Scale score at 3 months – no./total no. (%) | N=62; 2 missing | N=65; 1 missing | N=108; 1 missing | N=12; 0 missing | N=5; 0 missing |
| 0: No symptoms | 13/60 (21.7) | 8/64 (12.5) | 38/107 (35.5) | 3/12 (25.0) | 3/5 (60.0) |
| 1: No clinically significant disability | 18/60 (30.0) | 13/64 (20.3) | 37/107 (34.6) | 4/12 (33.3) | 2/5 (40.0) |
| 2: Slight disability | 13/60 (21.7) | 12/64 (18.8) | 11/107 (10.3) | 1/12 (8.3) | 0/5 (0.0) |
| 3: Moderate disability | 6/60 (10.0) | 18/64 (28.1) | 11/107 (10.3) | 1/12 (8.3) | 0/5 (0.0) |
| 4: Moderately severe disability | 6/60 (10.0) | 6/64 (9.4) | 9/107 (8.4) | 2/12 (16.7) | 0/5 (0.0) |
| 5: Severe disability | 1/60 (1.7) | 2/64 (3.1) | 0/107 (0.0) | 0/12 (0.0) | 0/5 (0.0) |
| 6: Dead | 3/60 (5.0) | 5/64 (7.8) | 1/107 (0.9) | 1/12 (8.3) | 0/5 (0.0) |

Table S4. Additional supplemental baseline data; not referred to in the manuscript

| Variable | Dexamethasone | Burr-hole craniostomy |
|---|--------------------------------|-----------------------|
| Residence prior to chronic subdural hematoma diagnosis – no./total no. (%) | | |
| At home | 118/127 (92.9) | 115/125 (92.0) |
| Residential home | 3/127 (2.4) | 3/125 (2.4) |
| Nursing home | 2/127 (1.6) | 2/125 (1.6) |
| Rehabilitation centre | 1/127 (0.8) | 1/125 (0.8) |
| Unknown | 3/127 (2.4) | 4/125 (3.2) |
| modified Rankin Scale score at admission – no./total no. (%) | | |
| 1: No clinically significant disability | 14/126 (11.1) | 17/124 (13.7) |
| 2: Slight disability | 18/126 (14.3) | 40/124 (32.3) |
| 3: Moderate disability | 16/126 (12.7) | 23/124 (18.5) |
| 4: Moderately severe disability | 72/126 (57.1) | 41/124 (33.1) |
| 5: Severe disability | 6/126 (4.8) | 3/124 (2.4) |
| Markwalder Grading Scale at discharge – no./total no. (%) | 6.25 (3.33-11.11) [¶] | |
| 0: Neurologically intact | 11/122 (9.0) | 52/110 (47.3) |
| 1: Alert, oriented. Mild symptoms such as headache. | 57/122 (46.7) | 44/110 (40.0) |
| 2: Drowsy or disoriented with variable deficits. | 48/122 (39.3) | 14/110 (12.7) |
| 3: Stuporous; responding to stimuli, severe focal signs. | 1/122 (0.8) | 0/110 (0.0) |
| 4: Comatose with absent motor responses | 0/122 (0.0) | 0/110 (0.0) |
| 5: Death | 5/122 (4.1) | 0/110 (0.0) |
| Markwalder Grading Scale at 2 weeks – no./total no. (%) | 2.50 (1.45-4.35) [¶] | |
| 0: Neurologically intact | 26/115 (22.6) | 49/114 (43.0) |
| 1: Alert, oriented. Mild symptoms such as headache. | 42/115 (36.5) | 47/114 (41.2) |
| 2: Drowsy or disoriented with variable deficits. | 42/115 (36.5) | 16/114 (14.0) |
| 3: Stuporous; responding to stimuli, severe focal signs. | 1/115 (0.9) | 0/114 (0.0) |
| 4: Comatose with absent motor responses | 0/115 (0.0) | 0/114 (0.0) |
| 5: Death | 4/115 (3.5) | 2/114 (1.8) |
| Ordinal modified Rankin Scale score at discharge – no./ total no. (%) | 3.57 (2.00-6.25) [¶] | |
| 0: No symptoms | 3/114 (2.6) | 22/104 (21.2) |
| 1: No clinically significant disability | 18/114 (15.8) | 34/104 (32.7) |
| 2: Slight disability | 19/114 (16.7) | 20/104 (19.2) |
| 3: Moderate disability | 34/114 (29.8) | 15/104 (14.4) |
| 4: Moderately severe disability | 35/114 (30.7) | 13/104 (12.5) |
| 5: Severe disability | 0/114 (0.0) | 0/104 (0.0) |
| 6: Dead | 5/114 (4.4) | 0/104 (0.0) |
| Ordinal modified Rankin Scale score at two weeks – no./ total no. (%) | 2.50 (1.47-4.35) [¶] | |
| 0: No symptoms | 14/111 (12.6) | 31/110 (28.2) |
| 1: No clinically significant disability | 19/111 (17.1) | 31/110 (28.2) |
| 2: Slight disability | 19/111 (17.1) | 24/110 (21.8) |
| 3: Moderate disability | 26/111 (23.4) | 9/110 (8.2) |
| 4: Moderately severe disability | 23/111 (20.7) | 11/110 (10.0) |
| 5: Severe disability | 6/111 (5.4) | 2/110 (1.8) |
| 6: Dead | 4/111 (3.6) | 2/110 (1.8) |

Table S4. *continued*

| Variable | Dexamethasone | Burr-hole craniotomy |
|---|----------------|----------------------|
| Other presenting symptoms – no./total no. (%) | | |
| Reflex abnormalities | 16/127 (12.6) | 4/125 (3.2) |
| Ataxia | 11/127 (8.7) | 11/125 (8.8) |
| Neglect/extinction | 16/127 (12.6) | 11/125 (8.8) |
| Apraxia | 5/127 (3.9) | 6/125 (4.8) |
| Hemianopsia | 5/127 (3.9) | 1/125 (0.8) |
| Decreased consciousness | 4/127 (3.1) | 4/125 (3.2) |
| Cranial nerve deficit | 10/127 (7.9) | 2/125 (1.6) |
| Diplopia | 1/127 (0.8) | 1/125 (0.8) |
| Sensible loss | 4/127 (3.1) | 8/125 (6.4) |
| Vertigo | 4/127 (3.1) | 6/125 (4.8) |
| Syncope | 1/127 (0.8) | 4/125 (3.2) |
| Incontinence | 7/127 (5.5) | 4/125 (3.2) |
| Duration between trauma and diagnosis – days | | |
| Median (min-max) | 42 (0-122) | 42 (0-147) |
| Mean ± standard deviation | 42.49 ± 26.26 | 45.61 ± 34.63 |
| Other coexisting medical conditions – no./total no. (%) | | |
| Heart valve disease | 11/127 (8.7) | 7/125 (5.6) |
| Deep venous thrombosis / Pulmonary embolism | 8/127 (6.3) | 7/125 (5.6) |
| Dementia | 7/127 (5.5) | 2/125 (1.6) |
| Chronic Obstructive Pulmonary Disease | 7/127 (5.5) | 11/125 (8.8) |
| Liver disease | 2/127 (1.6) | 2/125 (1.6) |
| Malignancy (current and/or in the past) | 25/127 (19.7%) | 16/125 (12.8) |
| Hypertension | 58/127 (45.7) | 59/125 (47.2) |
| Congestive heart failure | 10/127 (7.9) | 9/125 (7.2) |
| Hypercholesterolemia | 17/127 (13.4) | 16/125 (12.8) |
| Kidney disease | 11/127 (8.7) | 6/125 (4.8) |
| Epilepsy | 4/127 (3.1) | 0/125 (0.0) |
| Chronic subdural hematoma | 3/127 (2.4) | 1/125 (0.8) |
| Depression | 5/127 (3.9) | 2/125 (1.6) |
| Migraine | 2/127 (1.6) | 3/125 (2.4) |
| Hypothyroidism | 7/127 (5.5) | 3/125 (2.4) |
| Other medical history | 88/127 (69.3) | 75/125 (60.0) |
| Unilateral or bilateral chronic subdural hematoma – no./total no. (%) | | |
| Unilateral left | 42/127 (33.1) | 41/125 (32.8) |
| Unilateral right | 42/127 (33.1) | 51/125 (40.8) |
| Bilateral | 43/127 (33.9) | 33/125 (26.4) |
| Hematoma type – no./total no. (%) | | |
| Homogeneous | 69/127 (54.3) | 47/125 (37.6) |
| Laminar | 12/127 (9.4) | 15/125 (12.0) |
| Separated | 20/127 (15.7) | 24/125 (19.2) |
| Trabecular | 45/127 (35.4) | 42/125 (33.6) |
| Mixed | 4/127 (3.1) | 12/125 (9.6) |

Table S4. *continued*

| Variable | Dexamethasone | Burr-hole craniostomy |
|---|---------------|-----------------------|
| Type of antithrombotic medication – no./total no. (%) | | |
| Aspirin | 28/127 (22.0) | 23/125 (18.4) |
| Clopidogrel | 12/127 (9.4) | 11/125 (8.8) |
| Vitamin K antagonists | 30/127 (23.6) | 25/125 (20.0) |
| Directly acting oral anticoagulant (DOAC) | 9/127 (7.1) | 8/125 (6.4) |
| Heparin | 0/127 (0.0) | 1/125 (0.8) |
| Other | 3/127 (2.4) | 2/125 (1.6) |
| HbA1c at diagnosis | N=92 | N=83 |
| Median (min-max) | 41 (9.4-118) | 39 (8-91) |
| Mean ± standard deviation | 47.6 ± 19.4 | 42.1 ± 11.7 |

¶: Adjusted* common odds ratio

Table S5. Discharge supplementary material; not referred to in the manuscript

| Variable | Dexamethasone | Burr-hole craniostomy |
|---|----------------|-----------------------|
| Discharge destination – no./total no. (%) | | |
| Home | 62/126 (49.2) | 89/125 (71.2) |
| Residential home | 3/126 (2.4) | 9/125 (7.2) |
| Nursing home | 9/126 (7.1) | 8/125 (6.4) |
| Rehabilitation centre | 34/126 (27.0) | 9/125 (7.2) |
| Hospital | 13/126 (10.3) | 8/125 (6.4) |
| Deceased | 4/126 (3.2) | 0/125 (0.0) |
| Unknown | 1/126 (0.8) | 2/125 (1.6) |
| Glasgow Coma Scale score at discharge – no./total no. (%) | | |
| 13-15 | 121/122 (99.2) | 120/121 (99.2) |
| 9-12 | 1/122 (0.8) | 1/123 (0.8) |