Sensitivity of modern multislice CT for subarachnoid haemorrhage at incremental timepoints after headache onset: a 10-year analysis

Annabel Vincent,[1] Scott Pearson,[1] John W Pickering ,[1,2] James Weaver,[1] Leanne Toney,[1] Laura Hamill,[1] Michael Hurrell ,[3] Martin Than [1]

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[1]Christchurch Hospital Emergency Department, Canterbury District Health Board, Christchurch, Canterbury, New Zealand
[2]Department of Medicine, University of Otago Christchurch, Christchurch, New Zealand
[3]Christchurch Hospital Radiology Department, Canterbury District Health Board, Christchurch, Canterbury, New Zealand

Correspondence to
Dr Martin Than, Christchurch Hospital Emergency Department, Canterbury District Health Board, Christchurch 8140, Canterbury, New Zealand; martin@thanstedman.onmicrosoft.com

AV and SP contributed equally.

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ABSTRACT

Background CT performed within 6 hours of headache onset is highly sensitive for the detection of subarachnoid haemorrhage (SAH). Beyond this time frame, if the CT is negative for blood, a lumbar puncture is often performed. Technology improvements in image noise reduction, resolution and motion artefact have enhanced the performance of multislice CT (MSCT) and may have further improved sensitivity. We aimed to describe how the sensitivity to SAH of modern MSCT changes with time from headache onset.

Methods This was a retrospective analysis of electronic data collected as part of routine care among all patients presenting to Christchurch Hospital diagnosed with a SAH between 1 January 2008 and 31 December 2017. Patients were imaged with MSCT. The primary outcome was the proportion of patients with spontaneous aneurysmal SAH (identified via coding and confirmed by clinical and radiological records) that had a positive MSCT. The secondary outcome was the proportion of patients with any type of spontaneous SAH that had a positive MSCT.

Results There were 347 patients with an SAH of whom 260 were aneurysmal SAH. MSCT identified 253 (97.3%) of all aneurysmal SAH and 332 (95.7%) of all SAH. The sensitivity of MSCT was 99.6% (95% CI 97.6 to 100) for aneurysmal SAH and 99.0% (95% CI 97.1 to 99.8) for all SAH at 48 hours after headache onset. At 24 hours after headache onset, the sensitivity for aneurysmal SAH was 100% (95% CI 98.3 to 100).

Conclusion These data suggest that it may be possible to extend the timeframe from headache onset within which modern MSCT can be used to rule out aneurysmal SAH.

Key messages

What is already known on this subject

⇒ Prior literature suggests that a CT only (without subsequent lumbar puncture) is considered sufficiently sensitive to rule out subarachnoid haemorrhage (SAH) if performed within a 6-hour window from headache onset.

⇒ This time frame was based on pre-2008 third generation CT scanners.

⇒ Multislice CT (MSCT) has advanced technologically since 2008. It is unknown if modern MSCT is more sensitive for SAH than earlier scanners and if the 6-hour window can be lengthened.

What this study adds

⇒ Our single-centre retrospective study suggests that it may be possible to extend the timeframe from headache onset in which modern MSCT can be used to rule out aneurysmal SA.

INTRODUCTION

Headache is a common reason for presentation to EDs causing approximately 1%–2% of attendances.[1] While most headache presentations are due to benign pathologies such as tension headaches, subarachnoid haemorrhage (SAH) represents an important potentially life-threatening differential diagnosis. Atraumatic SAH is usually caused by blood leaking from a ruptured aneurysm but may occasionally result from benign, low pressure perimesencephalic haemorrhage or other vascular causes such as arterial dissection, vascular malformation or vasculitis.[2 3] SAH is one cause of sudden severe headaches that are described as maximal at onset. SAH causes around 10% of sudden onset, severe headaches.[4] Migraine and other more benign causes of headache that can mimic SAH are estimated to be 50 times more common than SAH.[5]

SAH is often a catastrophic diagnosis, with large morbidity and mortality. Up to 50% of patients die within 3 months without definitive early intervention, although there is regional variation in this rate.[6] SAH has an incidence of 6–8/100 000 persons/year,[1 7] and around 30% of survivors will have severe disabilities affecting their daily lives.[1]

Historically, studies suggested that CT detects as many as 93%–95% of SAH if the scan is performed within the first 24 hours after headache onset.[8] Given the life-threatening potential of the diagnosis, most patients therefore received a follow-up LP to bring the miss rate to within a margin that is more comfortable for most clinicians. Unfortunately, LP is unpleasant for the patient, timeconsuming, procedurally difficult in some cases, requires technical skill and has potential complications such as ongoing headache and local bleeding.[9–11]

The historical sensitivities listed previously were based on earlier generations of CT scanners than now available, but scanner technology has continually improved to make better detection of SAH possible. In a practice-changing study by Perry *et al*[12] in 2011 showed 100% sensitivity for the detection of SAH provided the scan was performed

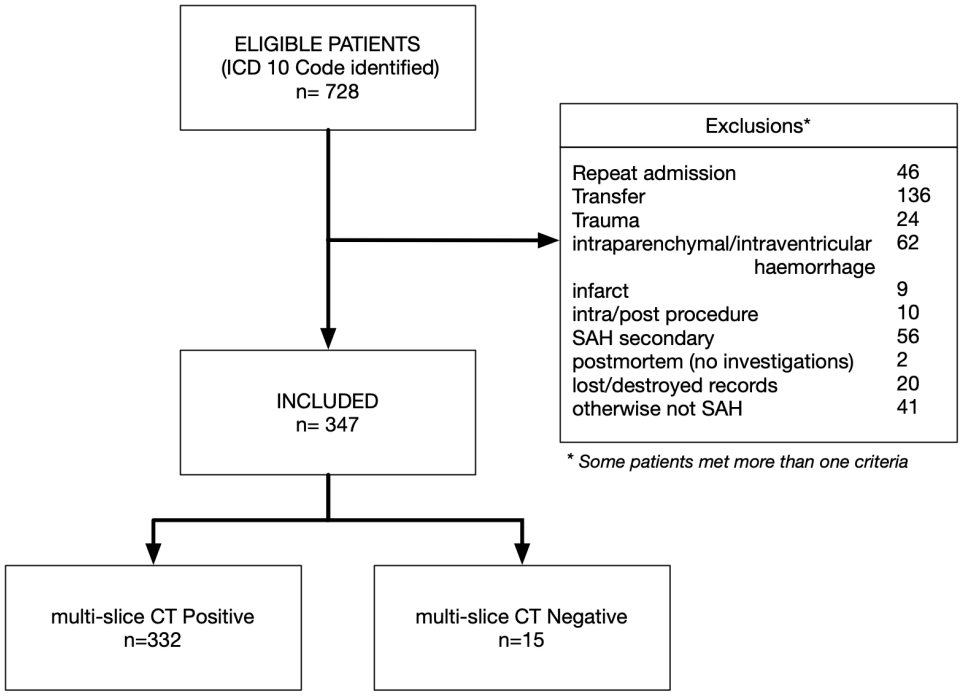

Figure 1 Flow chart showing application of exclusions and final MSCT results. MSCT, multislice CT; SAH, subarachnoid haemorrhage.

within 6 hours of headache onset. In this study, patients were only included in the analysis if they had a GCS of 15 and had no focal neurological deficits. This has essentially negated the need for routine LP after a negative CT, if performed within 6 hours of headache onset.

Perry *et al* used a wide range of third-generation multislice CT (MSCT), with between 4 and 320 slices/rotation, implying a range of image qualities. The protocols at the beginning of the study (2000–2002) used 5 mm slices for the posterior fossa and 10 mm for the remainder of the brain, which suffers from significant volume averaging when looking for small volume SAH. From 2002 to 2009, all sites adopted 5–7.5 mm cuts for the brain with 2.5–5 mm for the posterior fossa; although those slice thicknesses were an improvement, current scanners routinely provide 3 mm thick slices in this clinical setting. Since the Perry *et al* study, there have been further improvements for modern MSCT in image noise reduction, resolution and motion artefact that have continued to improve image quality.

We aimed to establish if modern MSCT could improve the sensitivity of SAH detection at sequential timepoints from symptom onset. This could potentially expand the time window within which CT alone can be used to exclude aneurysmal SAH.

METHODS

Setting and participants

This was a retrospective analysis of electronic data collected prospectively as part of routine care. It included all patients presenting to a single regional metropolitan ED (Christchurch Hospital, New Zealand) diagnosed with SAH between 1 January 2008 and 31 December 2017. Data extraction occurred during late 2018/early 2019 when the lead author was seconded to the Department of Emergency Medicine. The authors wished to review 10 years of data and required that mortality records to be complete beyond the duration of the data collection, hence because completion of mortality records takes some time, the decade 2008–2017 was chosen. Potentially eligible patients were identified from diagnostic coding using any of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (10 ICD-10) I60 SAH codes (I60.0–I60.9). Up to 20 ICD-10 codes per admission were retrieved. The study size was determined by the number of patients with these codes from 2008 to 2017.

Patients were excluded in the following order:

1. Cases determined to have been miscoded as SAH; for example, the described diagnosis was another haemorrhage type (such as intraparenchymal and intraventricular haemorrhage, but not SAH) recorded in the patient record or test results.
2. Clearly traumatic SAH.
3. The admission was a repeat SAH admission during the time period.
4. SAH found on postmortem in whom no MSCT was performed.
5. The day of onset of headache was not recorded.
6. Patient transferred to Christchurch Hospital from another hospital because of difficulties accessing radiology reports and clinical notes.
7. Patients with lost or destroyed records.

The exclusion criteria were first applied by AV and then reviewed by SP. No MSCT or clinical diagnoses were readjudicated. The identification of SAH was based on the radiology and clinical team record.

Patient and public involvement

No patients involved.

Index test

CT technology

The index test was a non-contrast MSCT of the brain. All patients during the study period were examined using either: (1) a 128-slice MSCT (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany) or (2) a 64-slice MSCT (GE VCT Lightspeed, GE Healthcare, Waukesha, Wisconsin, USA).

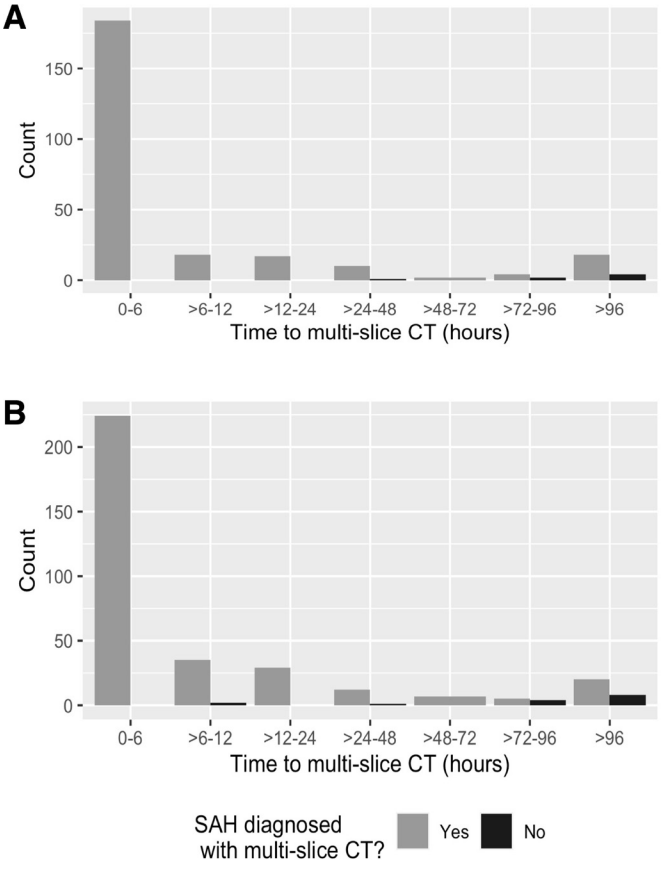

Figure 2 Time to MSCT. Panel A is for aneurysmal SAH; panel B for all SAH. SAH, subarachnoid haemorrhage.

From January 2008 to November 2012, standard CT slice width was 5 mm, and thereafter CT slice width was refined to 3 mm.

There are five generations of CT scanner that refer to the geometry of X-ray tube and detectors and the mechanical motion required to collect data. It is important to note that the term 'generation' refers to the order in which that CT scanner design has been introduced (each has a 'generation' number associated with it and that higher generation number does not mean a higher performance system (online supplemental appendix table 1). Third-generation scanners are those that use a wide fan-beam spiral acquisition. This technology has been available since 1975,[13] and it remains the standard imaging modality for acute care in developed nations. There are fourth-generation and fifth-generation scanners, but such scanners are not commonly available or used in the ED setting for acute imaging (online supplemental appendix table 1). Since the 1990s, notable refinements to scanning using third-generation scanners have occurred, with slip-ring gantries and multiple detector rows (multislice) enabling fast helical (volume) acquisitions.[13] Adding detector rows (in so-called multislice or multidetector scanners) rapidly expanded the utility of CT, with 64 slice machines becoming available in the late 1990s.[14] MSCT has evolved with technology improvements in image noise reduction, resolution and motion artefact. We describe the CT scanning during the study period (2008–2017) as modern MSCT because of specific improvements.[15] These improvements are described further:

1. Image noise reduction: made possible through improvements in detector signal-to-noise ratio and developments in reconstruction algorithms, such as raw data based iterative reconstruction.

Table 1 Demographics

	SAH not identified by MSCT (n=15)	MSCT identified SAH (n=332)	Overall (n=347)
Age			
Mean (SD)	60.8 (15.2)	59.9 (14.9)	59.9 (14.9)
Sex, n (%)			
F	3 (20.0)	218 (65.7)	224 (64.6)
Time to MSCT (complete hours), n (%)			
Median (min, max)	107 (7.4, 502)	1.5 (0.333, 913)	3.0 (0.333, 913)
0 to ≤6	0 (0.0)	224 (67.5)	224 (64.6)
>6 to ≤12	2 (13.3)	35 (10.5)	37 (10.7)
>12 to ≤24	0 (0.0)	29 (8.7)	29 (8.4)
>24 to ≤48	0 (0.0)	12 (3.6)	12 (3.7)
>48 to ≤72	1 (6.7)	7 (2.1)	8 (2.0)
>72 to ≤96	4 (26.7)	5 (1.5)	9 (2.6)
>96	8 (53.3)	20 (6.0)	28 (8.1)
Activity at time of onset, n (%)			
At rest	5 (33.3)	60 (18.0)	65 (18.6)
Awoken/onset during sleep	1 (6.7)	21 (6.3)	22 (6.3)
Coital	1 (6.7)	9 (2.7)	10 (2.9)
Exertional	1 (6.7)	24 (7.2)	25 (7.2)
Light activity	1 (6.7)	56 (17.1)	57 (16.6)
Not recorded	6 (40.0)	162 (48.8)	168 (48.4)
Location of headache, n (%)			
Cervical	1 (6.7)	2 (0.6)	3 (0.9)
Frontal	2 (13.3)	47 (14.1)	48 (13.8)
Global	1 (6.7)	13 (3.9)	14 (4.0)
Occipital	4 (56.7)	70 (21.0)	74 (21.3)
Temporoparietal	1 (6.7)	9 (2.7)	10 (2.9)
Occipitocervical	0 (0.0)	22 (6.6)	22 (6.3)
Not recorded	2 (13.3)	78 (24.0)	80 (23.1)
Not specified	4 (26.7)	91 (27.2)	96 (27.7)
Laterality of headache, n (%)			
Unilateral	1 (6.7)	23 (6.9)	24 (6.9)
Bilateral	3 (20.0)	30 (9.0)	33 (9.5)
Not recorded	2 (13.3)	81 (24.3)	83 (23.8)
Not specified	9 (60.0)	200 (59.9)	209 (59.9)
GCS at time of ED assessment, n (%)			
3	0 (0.0)	32 (9.6)	32 (9.2)
4	0 (0.0)	5 (1.5)	5 (1.4)
5	0 (0.0)	9 (2.7)	9 (2.6)
6	0 (0.0)	11 (3.3)	11 (3.2)
7	0 (0.0)	4 (1.2)	4 (1.1)
8	0 (0.0)	6 (1.8)	6 (1.7)
9	0 (0.0)	8 (2.4)	8 (2.3)
10	0 (0.0)	4 (1.2)	4 (1.2)
11	0 (0.0)	8 (2.4)	8 (2.3)
12	0 (0.0)	5 (1.5)	5 (1.4)
13	0 (0.0)	7 (2.1)	7 (2.0)
14	0 (0.0)	59 (17.7)	59 (17.0)
15	13 (86.7)	143 (43.1)	156 (45.0)
Missing	2 (13.3)	31 (9.3)	33 (9.5)
GCS-eyes, n (%)			
Mean (SD)	4.0 (0.0)	3.3 (1.2)	3.3 (1.1)
Missing	2 (13.3)	56 (16.8)	58 (16.6)
GCS-verbal, n (%)			
Mean (SD)	5.0 (0.0)	3.9 (1.6)	4.0 (1.6)

Continued

Table 1 Continued

	SAH not identified by MSCT (n=15)	MSCT identified SAH (n=332)	Overall (n=347)
Missing	2 (3.3)	55 (16.5)	57 (16.3)
GCS-motor, n (%)			
Mean (SD)	6.00 (0.0)	5.2 (1.7)	5.2 (1.7)
Missing	2 (13.3)	57 (17.1)	59 (16.9)
MRI – SAH present?, n (%)			
No	1 (6.7)	6 (1.8)	7 (2.0)
Possible	1 (6.7)	1 (0.3)	2 (0.6)
Yes	3 (20)	23 (6.9)	26 (7.4)
Not done	10 (66.7)	302 (90.9)	312 (89.9)
LP performed?, n (%)			
Yes	12 (75.0)	4 (1.2)	16 (4.6)
LP results: red cells first tube			
Median (min, max)	2.4e+10 (1.8e+07, 7.9e+10)	4.56e+10 (5.02e+09, 5.45e+11)	2.4e+10 (1.8e+07, 5.45e+11)
LP results: xanthochromia present, n (%)			
No	1 (6.7)	0 (0.0)	1 (0.3)
Yes	11 (73.3)	4 (1.2)	15 (4.3)
Treatment of SAH, n (%)			
Craniotomy/clipping	3 (20.0)	82 (24.6)	85 (25.0)
Endovascular/stenting	3 (20.0)	97 (29.2)	100 (28.8)
Nil	9 (60.0)	150 (45.2)	159 (45.8)
Missing	0 (0.0)	3 (0.9)	3 (0.9)
MSCT, n (%)			
GE VCT	8 (53.3)	165 (49.7)	173 (49.9)
Siemens Flash	7 (46.7)	167 (50.3)	174 (50.1)

MSCT, multislice CT; SAH, subarachnoid haemorrhage.

2. Increased resolution: finer high power X-ray tube focal spots, more compact detectors and multidetector row scanning have enhanced helical scanning techniques. Along with thinner slices and improved in-plane resolution, these advances facilitate routine imaging in three planes, improving diagnostic accuracy.
3. Reduced motion artefact: this has been achieved through faster gantry rotation, increased X-ray tube output capability and increased detector speed and sensitivity.

MSCT reporting

MSCT was considered positive if there was high-density material compatible with acute haemorrhage within the subarachnoid space and specifically the basal cisterns. It was considered negative if there was an absence of high-density material in the subarachnoid space. MSCT was considered indeterminate if there was degradation of image quality due to motion artefact or beam hardening. Imaging was interpreted by radiologists, including both general radiologists and neuroradiologists, prospectively as part of normal service provision. On some occasions, the initial interpretation was made by a radiology registrar in training with subsequent radiologist review. This is current normal practice and was normal practice at the time of the study. In four patients, the initial registrar report differed from the final radiologist report. The final, radiologist report was used for purposes of the test categorisation.

Routine approach to investigation

Patients were initially investigated, during the time period of the study, by MSCT. Where the MSCT was reported as negative, the next investigation was lumbar puncture. If the MSCT or lumbar puncture was considered positive, MSCT angiography was performed. On occasions, when doubt about aneurysm persisted or due to physician preference, the patient was investigated by MRI and MR angiography.

Reference standard

SAH was classified as being present if: (A) there was a coded ICD-10 diagnosis of SAH according to the ICD-10 codes described previously (in settings and participants) and (B) if this was confirmed in the radiology report and medical records (see exclusion criteria previously). Where SAH was confirmed, it was then subcategorised as aneurysmal or non-aneurysmal based on the radiological and clinical records.

Additional data collection

Additional cross checking of data was achieved by examining the Christchurch Hospital Neurosurgical Department patient database. Over the same time period, the Coronial database was examined to detect patients who had died suddenly in the community from SAH who may have had a related ED visit in the preceding 6 months. For secondary analyses, clinical data for identified patients were extracted from the Christchurch Hospital electronic health record (1 July 2009–31 December 2017) or retrieved from paper records (1 January 2008–30 June 2009).

Primary analysis

The primary outcome was the proportion of patients with spontaneous aneurysmal SAH that had a positive MSCT. The secondary outcome was the proportion of patients with any type of spontaneous SAH that had a positive MSCT. Time to MSCT was defined as the duration from headache onset until the time the MSCT was performed. The time of headache onset was retrieved from the health records and recorded as a date and time of day.

Process for missing time of headache onset data

Times of headache onset were sometimes missing from documentation, although the day of onset was always known. In these instances, an imputed time of onset was needed for calculation of time to MSCT.

We chose to use and present two methods for imputation: the first biased towards maximising the number of false negatives within shorter time frames from 0 hours, and the second with the opposite intent. If an exact time of onset of headache had been available for all patients, then the numbers of false negatives would lie between those of the two imputation methods.

In our approach biased towards maximising the number of early false negatives, missing time of onset data was imputed in one of two ways: (A) for headache onset known to be on the day of presentation, a time of onset of 30 min prior to presentation was used; (B) for headache onset known to be on a preceding day, 23:59 was used. In contrast, in our approach biased towards minimising false negatives, missing time of onset data was imputed to be 00:01 (1 min past midnight) on the day of headache onset. This imputation would systematically lengthen apparent time from onset to MSCT, diminishing false negatives across reported timepoints and increasing apparent safety.

Data analysis and statistical methods

Data are presented as n (%), mean (SD) or median (lower quartile – upper quartile), and statistical metrics with 95% CI. The

Table 2 Patients with non-diagnostic MSCT

	Age (years)	Sex	Test order	Time to MSCT (hours)*	Headache location	GCS	Aneurysm?	Aneurysm location	LP: final tube red cells x10^6/L	Xanthochromia present	MRI: SAH present?	Treatment	Outcome at discharge (MRS scale)
1	49	F	LP positive	10	Occipital	15	N		65000	Y	Not done	Nil	0. No symptoms at all
2	50	M	MRI positive	163–187	Not recorded	15	Y	Anterior communicating/ anterior cerebral	NA	NA	Possibly	Endovascular/ stenting	1. No significant disability despite symptoms; able to carry out all usual activities
3	72	F	LP positive	186–210	Occipital	15	Y	Internal Carotid Artery terminus	79000	Y	Not done	Nil	0. No symptoms at all
4	80	M	MRI positive	80–104	Not recorded	15	N			NA	Y	Nil	0. No symptoms at all
5	52	M	LP positive	85–109	Occipital	15	Y	Anterior communicating/ anterior cerebral	2000	Y	Not done	Endovascular/ stenting	0. No symptoms at all
6	62	F	LP positive	136–160	Frontal	15	Y	Anterior communicating/ anterior cerebral	18000	Y	Not done	Craniotomy/clipping	1. No significant disability despite symptoms; able to carry out all usual activities
7	61	M	LP positive	133–157	Not recorded	15	Y	Anterior communicating/ anterior cerebral	17000	Y	Not done	Endovascular/ stenting	1. No significant disability despite symptoms; able to carry out all usual activities
8	79	M	MRI positive	106–130	Not recorded	15	N		NA	NA	Y	Nil	3. Moderate disability; requiring some help, but able to walk without assistance
9	40	F	LP negative ->MRI positive	502–526	Global	15	N		4	N	Y	Nil	0. No symptoms at all
10	40	M	LP positive	7	Occipital	15	N		41000	Y	Not done	Nil	0. No symptoms at all
11	88	F	LP positive	369–393	Not recorded	15	NA		25000	Y	Not done	Nil	0. No symptoms at all
12	47	M	MRI –negative –>LP positive	139–163	Cervical	15	N		2900	Y	N	Nil	0. No symptoms at all
13	52	M	LP positive	90–114	Temporoparietal	15	Y	Anterior communicating/ anterior cerebral	13000	Y	Not done	Craniotomy/clipping	1. No significant disability despite symptoms; able to carry out all usual activities
14	58	F	LP positive	35–59	Not recorded	15	Y	Posterior communicating (including anterior choroidal)	37000	Y	Not done	Craniotomy/clipping	2. Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance
15	75	M	LP positive	93–117	Frontal	15	N		16000	Y	Not done	Nil	0. No symptoms at all

*Note that where the time of headache onset was not recorded (the date was always known), we show here the time to MSCT that was imputed (the last time which is the maximum time to MSCT) and 24 hours shorter (ie, the minimum time to MSCT). This is the real range of possible time to MSCT.
F, female; LP, lumbar puncture; M, male; MRS, modified Rankin scale; MSCT, multislice CT scan; N, no; NA, not applicable; Y, yes.;

sensitivity has been calculated for multiple time windows (0–6, 0–12, 0–24, 0–72 and 0–96 hours). Time 0 hour is the time of headache onset. Each specified window incorporates all patients who had an MSCT within that time frame. Within each window, we calculated the proportion of people with aneurysmal SAH (or all SAH) who had a positive MSCT. We express this as a percentage. The point estimates and CIs were calculated using 1000 bootstrapped samples. Statistical calculations were made in R V.3.5.1 (The R Foundation for Statistical Computing). The sample size was determined by the maximum time period possible with a consistent data collection approach and when MSCT was in use.

RESULTS

There were 728 admissions with an ICD-10 code for SAH. Of these, 46 were repeat admissions, and 136 were transfers from out of Christchurch. After all exclusions had been applied, there were 347 patients with a spontaneous SAH included in the analysis of whom 260 were aneurysmal SAH (figure 1). Patients were mostly female (64.6%) and older (mean age 59.9 years) (table 1). Examination of the Coroners mortality database revealed no sudden deaths with SAH of patients with a recent related ED presentation where a head MSCT was performed. There were 224 patients where the time of headache onset was not recorded. Of these, onset was the same day as arrival in the ED in 148 (66%). For these patients, the time of headache onset was therefore imputed (set) as 30 min prior to arrival time. For patients with headache onset during the preceding day, a time of 23:59 was imputed (used for the analysis). With this imputation strategy that maximised early false negatives, the median time from headache onset to MSCT was 3.0 hours (IQR 1.5–11.7 hours) (table 1 and figure 2). Overall, MSCT identified 253 (97.3%) of all aneurysmal SAH and 332 (95.7%) of all SAH. The 15 patients not identified with MSCT, of whom 7 (47%) were aneurysmal SAH, were diagnosed with SAH using a combination of Lumbar Puncture and/or MRI (table 2).

Primary analysis

The sensitivity of MSCT for aneurysmal SAH decreased as time to MSCT increased (figure 3A). At 6, 12, 24, 48, 72 and 96 hours post headache onset the sensitivity was 100% (98.0 to 100), 100% (98.2 to 100), 100% (98.3 to 100), 99.6% (97.6 to 100), 99.6% (97.6 to 100) and 98.7% (96.4 to 99.7), respectively (table 3). The number of patients within each time window are given in table 3. The sensitivity of MSCT for all SAH decreased as time to MSCT increased (figure 3B). The sensitivity for all SAH at 6, 12, 24, 48, 72 and 96 hours post headache onset was 100% (98.3 to 100), 99.2% (97.2 to 99.9), 99.3% (97.5 to 99.9), 99.0% (97.1 to 99.8), 99.0% (97.2 to 99.8) and 97.8% (95.5 to 99.1) respectively (table 3). There were only three patients presenting within 72 hours with a MSCT that was not diagnostic of any SAH. Two of these patients (table 2: patients 1 and 10) had non-aneurysmal SAH and did not require further treatment. The third patient had a normal MSCT at between 35 and 59 hours after headache onset (date but not onset time was recorded). They were subsequently found to have a posterior communicating artery aneurysm, which was managed with craniotomy and clipping.

There was no difference observed in the proportion of patients whose SAH was identified with MSCT between the two MSCT scanners used; overall, the 128-slice scanner was used 49.9% of the time and the 64-slice scanner 50.1%.

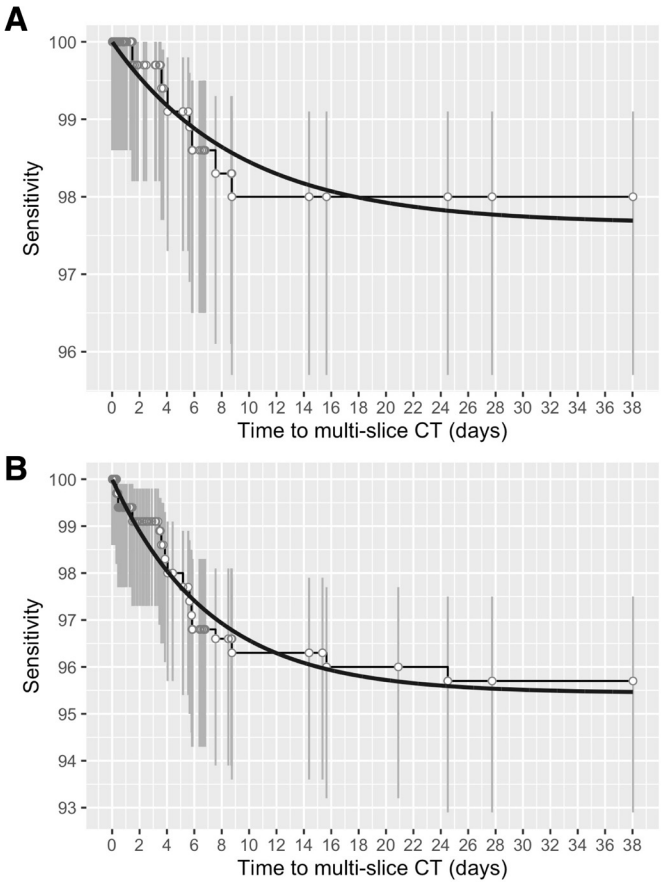

Figure 3 Sensitivity of time to MSCT. Panel A is for aneurysmal SAH; panel B is for all SAH. Points represent the actual sensitivity at each measurement time (eg, for panel B: sensitivity=100 * (347 – number with MSCT not true before time)/347). Grey vertical lines represent 95% CIs. Each step change to lower sensitivity is at the time at which the MSCT did not identify the SAH (ie, a false negative). The curved line is a non-linear least squares model best fit. MSCT, multislice CT; SAH, subarachnoid haemorrhage.

Sensitivity analysis

With the imputation strategy that minimised the number of false negatives of the time of headache onset the sensitivity of MSCT for aneurysmal SAH at 6, 12, 24, 48, 72 and 96 hours postheadache onset was 100% (94.8 to 100), 100% (96.8 to 100), 100% (98.2 to 100), 100% (98.4 to 100), 99.6% (97.6 to 100) and 99.6% (97.6 to 100), respectively (table 4). The small increase in sensitivity at a threshold of 48 hours compared with the imputation strategy that maximised false negatives (from 99.6% to 100%) is due to one false negative patient having a maximum possible time from headache onset to MSCT that was >48 hours.

DISCUSSION

Over a 10-year period, MSCT identified all aneurysmal SAHs when performed between 0 and 24 hours postsymptom onset. This is important because it potentially extends the timeframe from symptom onset during which a negative non-contrast MSCT might be used to rule out aneurysmal SAH. Overall, 95% of patients with any SAH were identified.

The overall sensitivity found in our research is consistent with other studies examining the sensitivity of modern MSCT for the detection of SAH in patients with sudden onset, severe headaches. Pooled sensitivity reported in the literature is 94%.[12 16 17]

Table 3 Diagnostic performance at set times post onset of headache using the imputation strategy that maximised early false negatives

Aneurysmal												
Time	<6 hours	≥6 hours	<12 hours	≥12 hours	<24 hours	≥24 hours	<48 hours	≥48 hours	<72 hours	≥72 hours	<96 hours	≥96 hours
MSCT positive	184	69	202	51	219	34	229	24	231	22	235	18
MSCT negative	0	7	0	7	0	7	1	6	1	6	3	4
Sensitivity (%) (95% CI)	100 (98.0 to 100)		100 (98.2 to 100)		100 (98.3 to 100)		99.6 (97.6 to 100)		99.6 (97.6 to 100)		98.7 (96.4 to 99.7)	
All patients												
Time	<6 hours	≥6 hours	<12 hours	≥12 hours	<24 hours	≥24 hours	<48 hours	≥48 hours	<72 hours	≥72 hours	<96 hours	≥96 hours
MSCT positive	224	108	259	73	288	44	300	32	307	25	312	20
MSCT negative	0	15	2	13	2	13	3	12	3	12	7	8
Sensitivity (%) (95% CI)	100 (98.3 to 100)		99.2 (97.2 to 99.9)		99.3 (97.5 to 99.9)		99.0 (97.1 to 99.8)		99.0 (97.2 to 99.8)		97.8 (95.5 to 99.1)	

MSCT, multislice CT.

Perry *et al* described a sensitivity of 100% for MSCT in detecting SAH within 6 hours of headache onset.[12] In a subsequent prospective implementation study, Perry *et al* reported a sensitivity of 95.5% although this study used a very broad definition of SAH.[18] Although lumbar puncture has long been considered an important second investigation for these patients if the CT is negative, there is evidence that clinicians are deviating from this advice given the low likelihood of detecting evidence of haemorrhage.[19 20] Other authors have also commented on the accuracy of MSCT to diagnose SAH. Cortnum *et al*[21] conducted a retrospective study between 2000 and 2005 describing 296 patients with diagnosed SAH. All were identified by MSCT with only one patient who presented at 6 days after headache onset requiring LP for diagnosis. Pouryahya *et al* also described a high sensitivity of MSCT in their retrospective data analysis between 2013 and 2018.[22] Although LP was performed in 388 patients in their series after initial normal non-contrast MSCT, only one patient was considered to have a true positive result, but on further imaging (MRI) had a small amount of intraventricular blood and no SAH and no aneurysm or any other vascular malformation. A meta-analysis of 22 studies suggested that LP was only likely to benefit a certain group of patients with pre-MSCT probability of 20% or higher.[23] Sayer *et al*[24] also describes a very high sensitivity of MSCT in their series although they had to exclude 15.6% of LPs as uninterpretable due to insufficient sample, incorrect storage or transport or sample loss.

There are five limitations to our analysis that we wish to highlight. First, it is retrospective, and second, we have relied on final diagnosis of SAH to identify participants. We believe it is unlikely that any patients presenting to hospital with SAH were not identified at initial attendance or on follow-up. This is because: (A) cross referencing with Neurosurgical Department and Coroners databases did not find patients who subsequently re-presented or suddenly died at home after their ED visit who had previously had a MSCT during their ED visit and (B) because Christchurch has one acute hospital, and any re-presentations of patients would likely return to the same hospital and therefore be included in the analysis. Nevertheless, we cannot completely rule out that an individual may have been seen in the ED, investigated for headache and discharged, travelled to another geographic location and subsequently admitted to hospital with SAH. This scenario is unlikely given the health structure in New Zealand and that Christchurch is the principle neurosurgical referral centre for the South Island of New Zealand. Third, the time of day of onset of headache was not available for many patients. Our imputation strategy that maximises the number of false negatives at shorter time frames underestimates the likely duration between headache onset and MSCT. Therefore, we underestimate the performance (sensitivity) of MSCT for each time band (and in particular for the 0–24 hour time window). The sensitivity analysis gives the maximum performance, which is very similar to minimum performance (100% vs 99.6%). Further research is needed incorporating additional prospectively collected data from multiple sites.

Fourth, we wish to emphasise that most of the diagnostic dilemma relates to individuals with sudden severe headache but normal level of consciousness. In our study, 156 patients had a GCS of 15. Of this group, 13 had an initial negative MSCT (all beyond the 0–24 hour time window) but subsequent investigations confirmed SAH (table 1). Further details are outlined in table 2 including the time from headache onset to time of MSCT.

Table 4 Sensitivity analysis

Aneurysmal												
Time	<6 hours	≥6 hours	<12 hours	≥12 hours	<24 hours	≥24 hours	<48 hours	≥48 hours	<72 hours	≥72 hours	<96 hours	≥96 hours
MSCT positive	70	183	117	136	198	55	224	29	230	23	231	22
MSCT negative	0	7	0	7	0	7	0	7	1	6	1	6
Sensitivity (%) (95% CI)	100 (94.8 to 100)		100 (96.8 to 100)		100 (98.2 to 100)		100 (98.4 to 100)		99.6 (97.6 to 100)		99.6 (97.6 to 100)	
All patients												
Time	<6 hours	≥6 hours	<12 hours	≥12 hours	<24 hours	≥24 hours	<48 hours	≥48 hours	<72 hours	≥72 hours	<96 hours	≥96 hours
MSCT positive	89	243	151	181	254	78	295	37	303	29	307	25
MSCT– negative	0	15	2	13	2	13	2	13	3	12	3	12
Sensitivity (%) (95% CI)	100 (95.9 to 100)		98.6 (95.4 to 99.8)		99.2 (97.2 to 99.9)		99.3 (97.6 to 99.6)		99.0 (97.2 to 99.8)		99.0 (97.2 to 99.8)	

Diagnostic performance at set times post onset of headache using the imputation strategy that minimised early false negatives.
MSCT, multislice CT.

Finally, there are relatively few patients who had MSCT beyond 24 hours from headache onset. Therefore, we recommend caution when interpreting the results pertaining to longer time windows (ie, beyond 24 hours).

CONCLUSION

Our data show a high sensitivity of modern MSCT non-contrast head scanning for detection of aneurysmal and non-aneurysmal SAH in patients with acute sudden onset severe headache if performed within 24 hours of headache onset. This suggests that it may be possible to extend the timeframe from symptom onset within which MSCT can be used to rule out aneurysmal SAH.

Twitter John W Pickering @kiwiskiNZ

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ORCID iDs
John W Pickering http://orcid.org/0000-0001-9475-0344
Michael Hurrell http://orcid.org/0000-0002-1595-2501
Martin Than http://orcid.org/0000-0001-9399-5227

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WEB APPENDIX

Supplementary Table 1

CT Scanner Generational Evolution

First generation	detectors: one type of beam: pencil-like x-ray beam tube-detector movements: translate-rotate duration of scan (average): 25-30 mins
Second generation	detectors: multiple (up to 30) type of beam: fan-shaped x-ray beam tube-detector movements: translate-rotate duration of scan (average): less than 90 sec
Third generation	detectors: multiple, originally 288; newer ones use over 700 arranged in an arc type of beam: fan-shaped x-ray beam tube-detector movements: rotate-rotate duration of scan (average): approximately 5 sec
Fourth generation	detectors: multiple (more than 2000) arranged in an outer ring which is fixed type of beam: fan-shaped x-ray beam tube-detector movements: rotate-fixed duration of scan (average): few seconds
Fifth generation*	Electron beam CT (limited to cardiac scanning and research) ultrafast, 33 millisecond scans multiple tungsten targets allow multibeam acquisitions Multiple detectors in an arc (varies from several hundred and more)
* Sinitsyn V.E., Achenbach S. (2004) Electron Beam Computed Tomography (EBCT). In: Oudkerk M. (eds) Coronary Radiology. Medical Radiology (Diagnostic Imaging). Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-662-06419-1_8	