Diagnostic modalities for the occult scaphoid fracture

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Chapter 8

Discussion and future perspectives

This thesis is about a patient who fell on an outstretched hand and sustained a scaphoid fracture that did not show on conventional radiographs. The question that arises is what the best diagnostic work-up will be for this patient. Although an enormous amount of research exists, we still do not have an evidence based answer to this question and hospitals use different protocols both nationally and internationally.(1-3) Due to inconsistent results published in literature, an ideal protocol could not be developed.
The aim of this thesis is to add valid and relevant data in the quest for the optimal protocol detecting scaphoid fractures that are not visible on conventional radiographs, the so-called occult scaphoid fractures.

In this thesis the diagnostic value of CT, MRI, bone scintigraphy and Tc-99m-HDP single photon emission computed tomography combined with low dose computed tomography (SPECT/CT) in occult scaphoid fractures is investigated.

We found the specificity of MRI to be less than reported in literature. We believe our study method, using healthy volunteers is more reliable compared to the studies that used different and imperfect reference standards and reported higher specificity.(4)
CT is specific, but has a lower sensitivity. Also observer variability is moderate. The clinical consequences of the missed fractures with CT are unknown. The radiation exposure of CT scan of the wrist is low. As it needs to be kept as low as possible, we advise to scan without a plaster cast.
Bone scintigraphy is a sensitive tool, but its specificity is lower which may result in overtreatment. Moreover, it is an invasive procedure, leads to radiation exposure and is time consuming.
SPECT/CT has similar objections. The diagnostic performance, however, seems promising. In our pilot study SPECT/CT has the potential to be more accurate than bone scintigraphy, as the diagnosis changed in three out of 10 patients using the anatomical information of the CT to discriminate between the scaphoid, other carpal bones and bone bruises. In future research it could serve as a superior reference standard.

Diagnostic challenges to overcome

If there is a clinically suspected scaphoid fracture (pain in the anatomic snuff box and/or pain on axial compression of the thumb and/or pain of the scaphoid tubercle), after a fall on an outstretched hand, there is a chance of 10 to 20 percent that an occult scaphoid fracture is present.(5-7) Therefore, advanced diagnostic methods such as CT, MRI and bone scintigraphy are used to rule out an occult fracture.

There are several issues in diagnosing occult fractures and the use of the different diagnostic modalities:

- It is unknown how many untreated occult fractures result in a symptomatic non-union.
- There is continuing inconsistency about if and how scaphoid fractures should be immobilised. Twenty years ago an above elbow cast is applied for 12 weeks, now some studies suggest a 4 weeks below elbow cast, without thump immobilisation.(8)
- Patients nowadays can be more demanding and litigation is infiltrating our decision models fast. (9) This potentially results in defensive medicine. However to what costs and to what extent of overtreatment?
- The main diagnostic challenge is that there is no 100% reliable reference standard available, which makes it difficult to conclude whether an outcome of a diagnostic modality is true or false.
- The low prevalence of occult fractures (10-20%) renders it relatively difficult to detect all fractures without overtreating multiple patients. Small percentages of false positive outcomes are magnified. (10)
- Diagnostic modalities are constantly evolving. MRI and CT imaging nowadays cannot be compared with several years ago as resolutions have improved dramatically. Comparison of diagnostic modality research results is there for complex and not always valid over time.

Pro's and cons of diagnostic solutions in this thesis

MRI

Literature reports that MRI has a specificity of 98-100% for ruling out scaphoid fractures (table 1). Sensitivity ranges between 88-98% (table 1). In this thesis the specificity of MRI is determined using healthy volunteers. As no 100% reliable reference standard is available we have turned it around and made sure we knew the diagnosis beforehand (no fracture). This resulted in a surprising high number of false positive outcomes and a specificity of 96%. The 96% may even be an overestimation as patients may have more abnormal signals on MRI after a fall on outstretched hand, which can be interpreted as a fracture. MRI is often used as a reference standard in many studies. In the light of the above findings, results of these studies also have to be interpreted with care.

We did not assess the sensitivity of MRI in this thesis. There are many studies evaluating the diagnostic performance of MRI and often report very high sensitivities (88-98%, table 1), but still without a valid reference standard. There may be room for a future study with optimized methodology to investigate the sensitivity of MRI, bearing in mind that adding value without a true reference standard will be difficult. Also, the ever improving quality of MRI's over time should then be taken into account.

CT

Studies concerning the diagnostic value of CT for diagnosing occult scaphoid fractures with sufficient power are scarce. In this thesis the diagnostic value of CT is investigated in a large patient population with clinically suspected occult scaphoid fractures. As a reference standard bone scintigraphy in combination with persistent clinical signs and radiograph follow up (6 weeks) was chosen. In our study, sensitivity of CT for diagnoses of an occult scaphoid fracture was 70% and specificity 99%. We hypothesize that the missed fractures had minimal dislocation as CT has high resolution and is superior in detecting dislocation of a fracture.(11) Accordingly, the fractures visible on follow up radiograph were all mid-waist scaphoid fractures without dislocation. If future studies can prove that these fractures will heal without a specific period of cast immobilisation, CT could be a very suitable diagnostic modality. Since CT is very specific it could save a lot of overtreatment when compared to repeated radiographs, bone scintigraphy and even MRI.

The interobserver agreement of CT for diagnosis of occult scaphoid fractures in the same patient population was moderate, which is quite disappointing. A different protocol with thinner CT slices may help improve this. It has to be taken into account that the interobserver agreement was determined in a population with clinical signs of a scaphoid fracture with ''no'' fracture on conventional radiographs, suggesting that if present at all, the fracture would not show much dislocation.

Another CT-related drawback is the use of radiation. Although radiation exposure of a CT of the wrist is low (0.02-0.03 mSv), patients need to know to what amount of radiation they are subjected too and ethically we need to keep the dosage As Low As Reasonably Achievable (ALARA). Scanning with a plaster cast results in an increased radiation exposure, as shown in this thesis. Therefore, we strongly advise to always make a CT without a plaster cast; it reduced radiation exposure by 90%. For comparison, bone scintigraphy of the wrist leads to a radiation exposure of 4 mSv and MRI none.

MRI, CT and bone scintigraphy in one patient population

For the first time in literature CT, MRI and bone scintigraphy were compared in the same patient population. Surprisingly there was only consistency in the negative results (all three scans showed no fracture). In the other patients the diagnostic modalities showed different results, consequently one or two had false outcomes in these patients. This illustrates the difficulty to investigate these diagnostic modalities without a true reference standard. None of these advanced diagnostic modalities meet the requirements to be the reference standard.

SPECT/CT

Finally, we have done a pilot study with SPECT/CT for diagnosing occult scaphoid fractures. In this pilot study the sample size was small (10 patients) and only one observer evaluated the SPECT/CT's. Bone scintigraphy was used for comparison. As location of the uptake of technetium-99 m hydroxymethylene diphosphonate was determined more accurate with SPECT/CT than with bone scintigraphy, SPECT/CT lead to different diagnoses in three out of the ten patients. SPECT/CT combines the high sensitivity of bone scintigraphy with the high specificity of CT and may in the end proof to be the most adequate for diagnosing occult scaphoid fractures. There are however considerable clinical and organizational disadvantages related to the SPECT/CT. It uses radiation and is time-consuming which makes it not very appropriate in daily practice. Still, it may be very suitable as a reference standard in further clinical research. Therefore more research is needed to determine the diagnostic value of SPECT/CT in a larger patient population.

Table 1. Pooled estimated results of the included reviews and meta-analyses.

	type	CT sensitivity	CT specificity	MRI sensitivity	MRI specificity	BS sensitivity	BS specificity
Mallee, 2015	Cochrane review	72	99	88	100	99	86
Yin, 2010	meta-analysis	93	99	96	99	97	89
Yin, 2012	meta-analyse*	85	100	98	100	98	84
Gemme, 2015	systematic review	83	97	96	98		
Carpenter, 2014	meta-analyse	83	97	95	98	90	81

** Including latent class analysis*

Review of literature

Many studies have been published concerning the subject of this thesis. We have performed a systematic review of reviews to give an overview of the knowledge nowadays, concerning diagnosis of scaphoid fractures (search strategy, figure 1). We chose to include reviews from 2010 as reviews concerning this subject are abundant. Moreover resolutions of CT and MRI have been improved, which makes it important that recent literature is included in the reviews. We have included and compared one Cochrane review, three meta-analysis and one systematic review. (exclusion chart, figure 2). The overall specificity and sensitivity results per modality, deducted from these reviews, are presented in table 1.

Mallee et al. (2015) have performed a Cochrane review for CT, MRI and bone scintigraphy.(5) They have included 11 studies of moderate to good quality. The pooled sensitivities and specificities are in Table 1. They found high heterogeneity in results between the studies as different reference standards were used. They concluded that statistically bone scintigraphy has the best diagnostic accuracy for detecting occult scaphoid fractures. However, due to a lower specificity it will lead to a relatively high rate of overtreatment.

Carpenter et al. (2014) have performed a meta-analysis for CT, MRI, bone scintigraphy, ultrasound, physical exam and patient history in relation to detecting occult scaphoid fractures.(12) They included 39 studies of low to moderate quality, concerning CT, MRI and bone scintigraphy. The pooled sensitivity

Figure 1. Search strategy

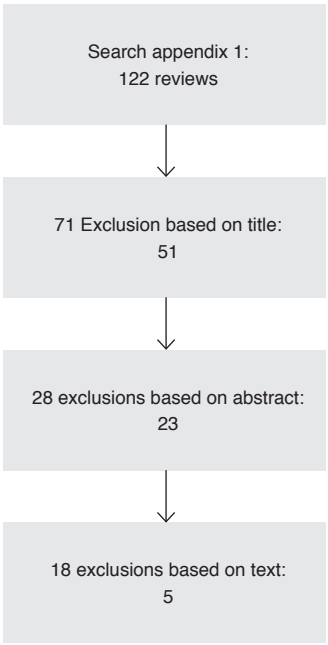
We searched Pubmed, Web of Science, Embase and Cochrane with the following search strategy:

("scaphoid bone fracture"[all fields] OR "scaphoid bone fractures"[all fields] OR "scaphoid bone injuries"[all fields] OR "scaphoid fracture"[all fields] OR "scaphoid fractures"[all fields] OR "scaphoid injuries"[all fields] OR "scaphoid injury"[all fields] OR "scaphoid stress fracture"[all fields] OR "scaphoid waist fracture"[all fields] OR "scaphoid waist fractures"[all fields] OR "scaphocapitate fracture syndrome"[all fields] OR "scaphocapitate fractures"[all fields] OR (("navicular body fracture"[all fields] OR "navicular body fractures"[all fields] OR "navicular bone fracture"[all fields] OR "navicular fracture"[all fields] OR "navicular fractures"[all fields] OR "navicular stress fracture"[all fields] OR "navicular stress fractures"[all fields] OR "navicular stress injuries"[all fields] OR "navicular stress injury"[all fields]) AND ("Hand"[mesh] OR "hand"[tw] OR "hands"[tw] OR "metacarpus"[tw] OR "metacarpal"[tw])) OR (("Scaphoid Bone"[mesh] OR "scaphoid"[ti] OR scaphoid*[ti] OR "scaphocapitate"[ti] OR ("navicular"[ti] AND ("Hand"[mesh] OR "hand"[tw] OR "hands"[tw] OR "metacarpus"[tw] OR "metacarpal"[tw]))) AND ("Fractures, Bone"[Mesh] OR "fracture"[ti] OR "fractures"[ti] OR "trauma"[ti] OR "injury"[ti] OR "injuries"[ti]))) AND ("Diagnosis"[Mesh:NoExp] OR "Diagnosis, Differential"[Mesh] OR "Diagnostic Imaging"[mesh:noexp] OR "Image Interpretation, Computer-Assisted"[mesh] OR "Magnetic Resonance Imaging"[mesh] OR "Multimodal Imaging"[mesh] OR "Radiography"[mesh] OR "Radionuclide Imaging"[mesh] OR "Tomography"[mesh] OR "Ultrasonography"[mesh] OR "diagnosis"[tiab] OR "diagnostic"[tiab] OR "diagnosis"[Subheading:NoExp] OR "radiography"[Subheading] OR "radionuclide imaging"[Subheading] OR "ultrasonography"[Subheading] OR "X-rays"[tw] OR "radiography"[tw] OR "radiology"[tw] OR "imaging"[tw] OR "computed tomography"[tw] OR "computer tomography"[tw] OR "computed assisted tomography"[tw] OR "computer assisted tomography"[tw] OR "CT-scan"[tw] OR "CAT-scan"[tw] OR "CT-scans"[tw] OR "CAT-scans"[tw] OR "magnetic resonance imaging"[tw] OR"MRI"[tw] OR "MR imaging"[tw] OR "scintigraphy"[tw] OR "SPECT"[tw] OR "SPECT-CT"[tw] OR "SPECTCT"[tw] OR "sonograms"[tw] OR "sonogram"[tw] OR "sonography"[tw] OR "sonographic"[tw] OR "ultrasound"[tw] OR "ultrasonography"[tw] OR "echography"[tw] OR "predictive value of tests"[mesh] OR "False Negative Reactions"[mesh] OR "False Positive Reactions"[mesh] OR "false negative"[all fields] OR "false positive"[all fields] OR "predictive value"[all fields] OR "Sensitivity and Specificity"[Mesh] OR "detection"[all fields] OR "detected"[all fields] OR "interobserver variability"[all fields] OR "inter-observer variability"[all fields] OR "intraobserver variability"[all fields] OR "intra-observer variability"[all fields] OR "clinical prediction"[tw] OR "sensitivity"[tw] OR "specificity"[tw]) AND (english[la] OR dutch[la]) NOT ("Animals"[mesh] NOT "Humans"[mesh]) AND ("2010/01/01"[PDAT] : "3000/12/31"[PDAT]) AND (systematic[sb] OR "review"[ptyp] OR "Meta-Analysis"[Publication Type] OR meta-analy*[tw] OR metaanaly*[tw] OR review*[ti])

and specificity for CT, MRI and bone scintigraphy are in Table 1. They concluded high heterogeneity between the studies. Also the majority of the studies investigated the value of MRI, which could have led to diagnostic research bias. They also discussed that there was no standardised inclusion criteria and different reference standards were used. They concluded MRI was the most accurate diagnostic tool; bone scintigraphy is only suitable for ruling out and CT only for ruling in scaphoid fractures.

Yin et al. (2010) performed a systematic review and meta-analysis for diagnostic accuracy of imaging modalities for suspected scaphoid fractures.(4) They investigated follow -up radiographs, CT, MRI and bone scintigraphy (search 1966-2008) and included 26 (24 concerning CT, MRI and bone scintigraphy) studies. Major conclusions were heterogeneity in methods, patient populations and different diagnostic protocols, between the included studies and lack of a true reference standard. They also marked possible confounders as these analyses are indirect (MRI, CT and bone scintigraphy were not tested in the same patient population). They concluded that MRI was the most accurate test; follow-up radiographs and CT may be less sensitive and bone scintigraphy is less specific. Yin et al. have repeated their search to 2011 and included six more studies and performed a latent class analysis.(6) The results of the pooled sensitivities and specificities of the meta-analysis (2010) and meta-analysis combined with latent class analysis (2012) are in Table 1. The latent class analysis and the inclusions of more recent literature did not change the results significantly. However, the latent class analysis was suboptimal as there was a lot of missing data.

Figure 2. Exclusion chart



Gemme et al. (2015) performed a systematic review for diagnosing scaphoid fractures.(13) They investigated the value of snuffbox tenderness, thumb compression, radiograph fat pad, radiographs 10-14 days later, CT and MRI. They included 75 studies of low to moderate quality. The results for CT and MRI are in Table 1. They concluded a significant level of heterogeneity, likely because there were no standardised inclusion criteria. Furthermore, there was a significant incorporation bias, double criteria standard and temporal bias. They concluded that MRI is the investigation of choice. However, in 3% of the emergency departments in the UK, MRI is available. As follow-up radiographs and physical exams are not sufficient to exclude a scaphoid fracture, advanced diagnostic follow up should be conducted.

Comparing our results to literature

Literature reports a specificity of 99% or higher for MRI.(5) Our MRI study, using healthy volunteers without a fracture or complaints, resulted in a specificity of 96%. The study design with healthy volunteers has advantages since no reference standard is needed. A potential explanation for the relatively low specificity might be the differences in reference standard. As other studies use imperfect reference standards it is possible that the false positive MRI's also had a false positive reference standard. Most studies used a combination of clinical findings and follow up radiography. It is known that clinical findings are not specific.(13,14) Contusions of the scaphoid may have had a positive MRI and positive clinical findings without a present fracture. On the other hand, since only non-fractured wrists are reviewed a spectrum bias may have been introduced in our study.

The results of the comparison of CT scan with bone scintigraphy for detection of occult scaphoid fractures are consistent with those of previous publications.(15,16) CT is specific, however not a very sensitive diagnostic modality. We also found a moderate interobserver agreement. One other study investigated the interobserver agreement in this patient population and they found substantial agreement.(7) The difference might be the result of a different CT protocol with thinner slices.

Since it is important not to miss any fractures, CT does not seem to be the investigation of choice. However, CT has numeral advantages. Its availability is better than that of MRI and bone scintigraphy and it is less time-consuming. Also, since specificity is high, there is little overtreatment. An important question is to what extent the missed fractures with CT will lead to an adverse outcome. Displacement on scaphoid radiographs is associated with a higher rate of non-unions.(11) Unfortunately no study has been performed assessing the rate of non-unions with different fracture patterns on CT. Moreover there is no study evaluating the rate of non-unions in patients with a clinically suspected scaphoid fractures, a negative radiograph and negative CT, which received no treatment.

Bone scintigraphy is a sensitive tool, however it has a lower specificity compared to MRI and CT. Our results are comparable to the reviews published prior to our study. Bone scintigraphy is less favorable because it is time-consuming, invasive, expensive and it leads to radiation exposure. If we add the disadvantage of its lower specificity, it is not the most suitable diagnostic tool, despite its high sensitivity. It could serve as a reference standard in future studies, especially when combined with SPECT/CT as we showed in our pilot study. Only one recent study of Querellou et al. evaluated 57 patients with a clinically suspected scaphoid fracture and a negative conventional radiograph, using

SPECT/CT and MRI.(17) They concluded that SPECT/CT is more sensitive for a fracture in the carpal area, as it detected 10 more carpal fractures than MRI.

In this thesis we compared CT, MRI and bone scintigraphy on the same population, which is unique. There were no consistent outcomes between the three diagnostic modalities, which illustrates the shortcomings of every diagnostic modality.

Repeated radiographs have not been investigated in this thesis although many clinics still use these repeated radiographs for assessing patients with a clinically suspected scaphoid fracture.(1-3) Ultrasound is an alternative diagnostic modality which we did not investigate. However, there is sufficient literature that demonstrates ultrasound and repeated radiographs to be inadequate for ruling out scaphoid fractures. Yin et al. assessed the value of repeated radiographs in their meta-analysis combined with the latent class analysis.(6) Sensitivity was not sufficient especially when MRI was used as a reference standard. In 2016 this was underlined with an observer study were 81 orthopedic surgeons assessed repeated radiographs. They found a low agreement and concluded repeated radiographs are not adequate.(18) The value of ultrasound has been assessed in a review. Four studies had very small sample sizes. Only one study included 58 patients and used repeated radiographs at 10-14 days as a reference standard. Sensitivity was only 50%. They concluded ultrasound is not sensitive enough to rule out scaphoid fractures. Of course there may be room for ultrasound in the absence of other diagnostics such as MRI, CT or bone scintigraphy.(19)

Future perspectives

Obviously, the major problem in investigating advanced imaging techniques for detecting occult scaphoid fractures is the absence of a true reference standard and the low prevalence of true fractures. Statistical compensation for this lack of standard may proof helpful.
Latent class analysis may provide a more accurate estimation of the diagnostic characteristics in these advanced imaging techniques without a true reference standard. However, for an adequate analysis, study methods still need to be optimized and more patient variables (age, sports, outcome etc) are needed for a proper latent class analysis.(6)
As for the low prevalence of true fractures, the pre-test probability of a fracture can be influenced by incorporating a clinical prediction rule.(14,20)
Furthermore, the value of SPECT/CT is promising. Although SPECT/CT has considerable disadvantages (costs, time-consuming, radiation exposure), it may have a function as a reference standard in studies.
In future studies we need to combine the best possible reference standard, a clinical prediction rule and results interpreted with latent class analysis. Only then we may obtain more comparable and more reliable results.

Moreover we need to interpret the results in clinical perspective.Radiographically unstable and proximal pole fractures are associated with a higher rate of non-union. (21-25) Non-displaced fractures on conventional radiographs will heal with conservative treatment in 90-100%.(21,23) However, the occult fracture seems a different entity and it is not known how important treatment of an occult scaphoid fracture is. In perspective of this thesis, the importance of the treatment of potentially missed fractures on CT, MRI and bone scintigraphy is not known. It can be hypothesized that fractures missed with CT will probably be minimal dislocated and will have a good healing tendency anyway. The ultimate goal remains uncomplicated fracture healing and prevention of non-unions. Although CT misses between 20 to 30% of the occult scaphoid fractures compared to MRI and bone scintigraphy, the clinical consequences may be far less impressive than these percentages.

In this context it is interesting to look at the retrospective study of Reigstad et al., ''Scaphoid non-unions, where do they come from? The epidemiology and initial presentation of 270 scaphoid non-unions''. (26) In this study 270 patients with scaphoid non-unions were evaluated for their clinical presentation. Surprisingly only 148 (55%) patients with a non-union had initially visited a doctor. In 60 patients (22%) the diagnosis was missed on initial radiography and instead the patients were diagnosed with a sprain. These 60 patients with an occult scaphoid fracture could have been diagnosed with a scaphoid fracture if additional imaging had been performed, however, probably without consequences for their final outcome. The incidence of non-unions is 2,5 per 100.000 persons.(26) Therefore, 0,5 per 100.000 scaphoid non-unions were at initial presentation occult (assuming the 22% occult fractures of the study above). The incidence of scaphoid fractures is approximately 30 per 100.000.(27) As 25% of clinical suspected scaphoid fractures have a fracture, the incidence of suspected scaphoid fractures is 120 per 100.000. Therefore, 0,42% (0,5/120) of patients with a suspected scaphoid fracture can have benefit of additional imaging. The difference between the sensitivity of CT and MRI is around 20-30%, consequently in 0,1% of patients with a suspected scaphoid fracture, that can be missed with CT compared to MRI, has potentially a fracture that can lead to a non-union. Moreover there is the

possibility that CT only misses the fractures with minimal dislocation and good healing tendency and will detect the fractures with the potential of becoming a non-union.

Clinical implications for the diagnosis of a scaphoid fracture

- When using CT there is a chance that fractures are missed.
- CT is less sensitive than MRI and bone scintigraphy and has moderate observer agreement. The clinical implications of this are currently unknown.
- If a CT scan is indicated, it is advised to make a CT of the wrist without a plaster cast in order to keep radiation exposure as low as possible.
- When using MRI there is a chance that fractures are missed.
- The specificity of MRI may be overestimated in literature.
- Bone scintigraphy is sensitive but less specific. When using bone scintigraphy there is a relatively high chance of overtreatment.
- Also, bone scintigraphy is time-consuming, invasive and radiation exposure is a disadvantage.

As no true reference standard is available and results can be magnified due to a low prevalence of true fractures, care has to be taken into account when interpreting results of any study concerning this topic. Future research has to focus on latent class analysis and study methods should be optimized. In order to obtain comparable data a prospective study for SPECT/CT is suggested as this could serve as a reference standard. Future research has to focus on the risk factors for developing non-union after occult scaphoid fractures, before we can develop an ultimate protocol.

Conclusion

In conclusion, in case of an clinically suspected radiographic occult scaphoid fracture, bone scintigraphy is very suitable diagnostic modality for detecting occult scaphoid fractures, however its radiation exposure is relatively high and the lesser specificity will lead to overtreatment. The most practical radiologic workup in the light of the present research would be MRI or CT. The chance of undertreatment should however be taken into account.

Therefore, clinical presentation, individual patient characteristics and fracture patterns will co-determinate the injury management. The treating physician holds final responsibility for the individualised further diagnostic follow-up and treatment strategy, as MRI, CT and bone scintigrapy individually are not 100% conclusive.

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