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Development of the Pediatric Elbow Trauma (PET) rules as a decision rule for radiography in traumatic elbow injuries: A study protocol

Background: Traumatic elbow injuries in children occur frequently and are among the most common traumatic injuries seen on the Emergency Department (ED) and in general practice. The use of a validated decision rule to enhance selective radiography in pediatric patients with possible elbow fractures may reduce unnecessary exposure to radiation in children. Additionally, a decision rule may improve the quality of care for pediatric traumatic elbow injuries by reducing ED times and health care costs.

Methods/design: This study is designed as a multicenter prospective cohort study. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will initially determine clinical parameters that provide a possible predictive value for elbow fractures. Four hundred children between the ages of 2 and 17 years visiting the ED with pain following elbow trauma will then be included. The clinical parameters will be collected via patient history and physical examination. Elbow radiographs will be obtained in all patients to identify fractures. The data will be processed in a multivariable logistic regression analysis to determine which clinical parameters predict the presence of an elbow fracture. Only the clinical parameters that predict a fracture will be used to formulate the new decision rule: the pediatric elbow trauma (PET) rules. Internal validation of the prediction model will take place after inclusion is complete and by means of a bootstrap analysis on the acquired data. A calculation will be made to determine how many radiographs can potentially be reduced by applying the PET-rules and a cost-analysis will be performed.

Ethics and dissemination

The study will be conducted according to the principles of the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO, valid since July 1st 2021). This Medical Research Ethics Committees United stated on 16 may 2022 that The Medical Research Involving Human Act (WMO) does not apply to this study and an official approval by the committee is not required, reference number; project W22.086.

Level of evidence: diagnostic study level 2

Introduction

Elbow fractures are defined as fracture of the distal part of the humerus and/or proximal part of the radius and/or proximal part of the ulna. Forty percent to 60% of all boys and 25% to 40% of all girls will visit the emergency care with a fracture during their childhood.(1) Pediatric elbow fractures are amongst the most common injuries seen on the ED(1). Incorrect diagnosis and treatment can lead to undesirable pain and decreased range of motion during adult life.

Plain radiography of the elbow is used to visualize the suspect diagnosis of a fracture. Hence, every child with a traumatic injury to the elbow visiting the ED must endure a very small but potentially harmful dosage of radiation, even though the majority of these patients have no fracture. A decision rule may be useful to reduce the number of unnecessary radiographs.

More than a decade ago, the research group of Appelboam A. et al(2) developed the elbow extension test, a decision rule to enhance selective radiography and decrease the risks of radiation by reducing the number of unnecessary X-rays. The use of this decision rule ultimately led to an absolute reduction in the number of unnecessary plain radiography taken from children. This trend is also seen in other decision rules designed for injuries to other joints, such as the ankle, knee, wrist and neck.(3–7)

Recently, a research group in Amsterdam developed the Amsterdam Pediatric Wrist Rules (APWR) (8,9), the first validated decision rule for pediatric acute wrist trauma. With the implementation of the APWR, an absolute reduction of 19% of the unnecessary radiographs

was seen. These data highlight a knowledge gap and opportunity for the development of a decision rule for pediatric elbow fractures.

Our research objective is to develop, validate and implement an extended decision rule for pediatric elbow fractures (the Pediatric Elbow Trauma rules) to improve selective radiographic imaging and reduce unnecessary exposure to radiation in children. Furthermore, we aim to improve the quality of care for children who present at the emergency care with an injury of the elbow by reducing the waiting times and health care costs.

Methods

Study design

This is a multi-center prospective observational study of pediatric patients who visit the emergency department with a traumatic elbow injury. The data will be collected in four different hospitals; one academic hospital, two large teaching hospitals and one general hospital.

The first part of this research is the development of the decision rule with use of clinical parameters obtained from baseline patient characteristics, patient interview and physical examination. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will determine which clinical parameters provide a possible predictive value for elbow fractures. We will collect all clinical parameters (originating from the expert panel) via the patient history and physical examination from all patients. All patients will get radiographs of the affected elbows and will be provided emergency care according to local

hospital protocols. These patient data will be processed in a multivariable logistic regression analysis to determine the clinical parameters that predict the presence or absence of an elbow fracture. Only the clinical parameters which significantly predict a fracture, within this prediction model, will be used to formulate the new decision rule.

In the second part of this research, the newly developed decision rule will undergo internal validation using the data gathered in the first part of the research. At the same time we will determine the primary outcome measurements: the potential absolute reduction in the number of X-ray examinations, a calculation detailing how much costs have been saved by taking more selective X-rays and a calculation on time saved during an ED visit.

Study population

The study population is defined as all consecutive children/adolescents aged two to seventeen years who visit the emergency department of one of the participating hospitals with pain following elbow trauma. The anatomical region of the elbow is defined as the bony and articular surfaces of the distal humerus, the proximal ulna and the proximal radius.(10) A traumatic injury is defined as any direct or indirect low- or high-energetic trauma involving the elbow. A full list describing the inclusion and exclusion criteria is given in table 1.

Inclusion criteria
- Patients aged between 2 and 17 years - Traumatic injury of the elbow (maximum 72 hrs prior to presentation on the emergency department) - Pain in the anatomical region of the elbow joint

Exclusion criteria
- Pre-existent neurological pathology, genetic disorders and/or bone disorders in the affected limb - Current ipsilateral fracture of wrist or shoulder - Previous fracture of the ipsilateral upper extremity (from clavicle to distal phalanges) <3 months - Patients referred from another hospital where X- rays of the elbow were performed - A multitrauma patient (Injury severity score > 16) - Mentally disabled children - Unable to communicate in Dutch or English

Table 1: Inclusion and exclusion criteria used during the selection of pediatric patients in this study.

Sample size

A sample size calculation is not applicable due to the multivariable character of this study; a convenience sample will therefore be used. A logistic regression analysis is used to determine the potential variables for the final decision rule. The variance between outcomes per variable within a regression analysis dictates the sample size per variable. The variance between outcomes for the potential variables in the decision rule is estimated to be very small (predominantly yes/no answers). Jenkins et al, Riley et al and Steyerberg et al (11–13) described a detailed calculation for an adequate sample size in clinical decision/prediction models. Based on their recommendations, we aim to include 400 patients for our study. To summarize: on average 8-12 participants are needed per variable to ensure a valid prediction can be made concerning the variables' discriminative value. To increase the accuracy of the prediction model, we will focus on 10 predictive potential variables with a high a-priori chance of underlying traumatic injury to the bone. Therefore, we will need to include a

minimum of 100 patients (10 variables x 10 patients). To ensure an accurate internal validation for our updated clinical decision rule a minimum of 300 patients must be included.(13) Based on these estimates we have chosen to include 400 patients for our research.

Statistical analysis

The data from standardized electronic case report forms (CRFs) will be used to develop the prediction model, by using a multistep logistic multivariable analysis in a shrinkage model. During the first step, a univariate logistic regression analysis will be used to estimate the regression coefficients and analyze the correlation between a variable and the presence or absence of a fracture. The regression coefficients will be processed, in the second step, through a multivariate shrinkage model to establish significant regression coefficients and generate a relative risk score per variable. Sensitivity, specificity, positive predictive value and negative predictive values will be gathered. The accuracy of the model will be estimated by a goodness of fit test with a graphical calibration curve and a receiver operating characteristics (ROC) curve with a discriminative curve. Overfitting will be controlled by calculating the optimism estimation of the C-statistic. Internal validation will be performed through bootstrapping to estimate overfitting and adjust the model accordingly. The final decision rule will be presented as a simplified risk score for easy use by emergency care physicians.

Missing data

We will use three strategies to avoid or adequately substitute potential missing data: (1) optimizing the study design and implementation methods to avoid missing data, such as;

training doctors, creating simplified CRFs and adhering to normal treatment protocol, (2) sending regular updates to all participating hospitals, (3) investigating patterns of missing data to allow analyses to explore potential reasons for missing data and impute missing values by chained equations to avoid bias.

Study procedures

Data collection will take place starting November 2022 and will be completed after including 400 patients, preferably within a 2-year period. All pediatric patients presenting to the emergency department following a traumatic injury of the elbow will receive care as usual according to hospital protocol. To develop the decision rule, we will collect patient characteristics in a standardized fashion during the interview and physical examination. A standardized electronic case report form will be generated to collect the data during the participant's visit. The attending (orthopedic/surgical) physicians collecting the data will receive instructions and training before recruiting participants to the study. Possible predictive clinical parameters are patient age and gender, point tenderness at lateral or medial distal humerus, radial head, olecranon, limited range of motion for supination/pronation/flexion and extension, hypoesthesia of the lower arm, increased capillary refill test, visible hematoma and trauma injury mechanism. All participants will receive plain elbow radiographs, according to Dutch guidelines; anterior-posterior view with the hand in anatomical position and a lateral view with the thumb in upwards position.(14) Additional imaging for associated injuries or to confirm suspected diagnosis will be performed at the discretion of the treating orthopedic or trauma physician.

Primary outcome parameters

Our primary outcome measurement is the existence of a fracture on the conventional x-ray diagnosed by a musculoskeletal radiologist. A fracture is defined as a partial or complete disruption of one or more of the cortices in the ulna, radius or humerus within the elbow region and all epiphysial growth plate injuries visible on AP or lateral view. Avulsions or displacement of apophyseal growth plates are also defined as a fracture. All additional imaging (radiography, magnetic resonance imaging or computed tomography) performed by the on-call physician and radiologist will be taken into account when diagnosing the fracture.

Our primary outcome, a fracture of the elbow, will be measured after inclusion of all 400 patients. All participants will receive plain elbow radiography. After inclusion has ended all conventional radiographs will be gathered for final inspection. This will be done by two musculoskeletal radiologist in consensual agreement and blinded to the clinical parameters and medical history of the patient. The two musculoskeletal radiologist will provide a detailed diagnostic report, after reaching consensus, for every radiography performed on our patients. This final report will dictate the presence or absence of a fracture of the elbow after traumatic injury to the elbow in the pediatric patient.

Withdrawal of individual subjects

Participants can leave the study at any time for any reason if they wish to do so without any consequences. The principal investigator or treating physician can decide to withdraw a subject from the study for urgent medical reasons.

Patient and public involvement

The patients and public were not involved in the design of this study protocol

Ethical consideration

Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO, valid since July 1st 2021). This Medical Research Ethics Committees United stated on 16 may 2022 that The Medical Research Involving Human Act (WMO) does not apply to this study and that an official approval by the committee is not required, reference number; project W22.086.

Recruitment and consent

Potential participants and/or the parents or legal guardians of the participants will be asked to join our study by the physician on call in the Emergency Department prior to regular diagnosis and treatment. Verbal informed consent will be given. Participants have no obligation to participate and will receive diagnosis and treatment as normal. Participants who are willing to join will receive similar treatment, the only difference is that clinical parameters recorded during patient interview and physical examination will be more extensive and will be recorded in a case report form.

Administrative aspects

Handling and storage of data and documents

All acquired patient-related data will be anonymously coded with a referencing legend for safe used by members of the research team. Research data will be stored in a database (SPSS version 25 and Castor EDC and SMS) and can be traced to individual persons only by authorized personnel. The personnel authorized to view the database include the members of the research team, members of the health care inspection, and members of the Medical Ethics Committee. Review of the data may be necessary to ensure the reliability and quality of the research. The handling of personal data is in compliance with the Dutch act on Implementation of the General Data protection Regulation (in Dutch: 'Wet Algemene Verordening Gegevensbescherming persoonsgegevens'), the EU General Data Protection Regulation and the privacy regulation of all involved hospitals.

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Development and validation of the Pediatric Elbow Trauma (PET) rules as a decision rule for radiography in traumatic elbow injuries: A study protocol

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Keywords: Pediatric orthopedics; Radiography; decision rule

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Competing interests statement

All authors declare that they have no competing interests.

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Contributor statement

In the process of creating the manuscript, the seven authors fulfilled the following roles and tasks:

1. TFF *Main author*; setup the design of the study, recruiting an expert panel, conception and writing of the manuscript
2. CJA *Study designer*; conception and design of the study, provided orthopedic and scientific expertise and critical revisions to the study protocol.
3. B *Expert panel*; providing critical revisions and help with interpretation of data
4. PBH *Expert panel*; providing critical revisions and help with interpretation of data
5. NWL *Expert panel*; providing critical revisions and help with interpretation of data
6. LC *Legal counsel and statistical help*; aided in legal issues, assisted with administration and data management, provided statistical help.
7. D *Final* author; conception and design of the study, provided orthopedic and scientific expertise and critical revisions to the study protocol. Final author of the manuscript.

Acknowledgements

None.

Abstract

Background: Traumatic elbow injuries in children occur frequently and are among the most common traumatic injuries seen on the Emergency Department (ED) and in general practice. The use of a validated decision rule to enhance selective radiography in pediatric patients with possible elbow fractures may reduce unnecessary exposure to radiation in children.

Method and analysis: This study is designed as a multicenter prospective cohort study. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will initially determine clinical parameters that provide a possible predictive value for elbow fractures. Four hundred children between the ages of 2 and 17 years visiting the ED with pain following elbow trauma will then be included. The clinical parameters will be collected via patient history and physical examination. Elbow radiographs will be obtained in all patients to identify fractures. The data will be processed in a multivariable logistic regression analysis to determine which clinical parameters predict the presence of an elbow fracture. Only the clinical parameters that predict a fracture will be used to formulate the new decision rule: the pediatric elbow trauma (PET) rules. Internal validation of the prediction model will take place after inclusion is complete and by means of a bootstrap analysis on the acquired data. A calculation will be made to determine how many radiographs can potentially be reduced by applying the PET-rules and a cost-analysis will be performed.

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The study will be conducted according to the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act. The Medical Research Ethics Committees United stated on 16 may 2022 that The Medical Research Involving Human Act (WMO) does not apply to this study and an official approval by the committee is not required, reference number; project W22.086.

SUMMARY

What is known about the subject?

Pediatric elbow fractures are very common and only one diagnostic decision rule is available. Every child will have undergone a plain radiography to check for possible fractures.

What this study hopes to add?

To modernize the diagnostic decision rule for pediatric elbow fracture and increase its sensitivity and to reduce the unnecessary radiation exposure to children on the emergency care when taking an overabundant radiography.

How this study might affect research, practice and policy?

To ensure not every child undergoes a radiography, but only those with a high chance of elbow fracture decided through our decision rule.

Introduction

Elbow fractures are defined as fracture of the distal part of the humerus and/or proximal part of the radius and/or proximal part of the ulna. Forty percent to 60% of all boys and 25% to 40% of all girls will visit the emergency care with a fracture during their childhood.(1) Pediatric elbow fractures are amongst the most common injuries seen on the ED(1). Incorrect diagnosis and treatment can lead to undesirable pain and decreased range of motion during adult life.

Plain radiography of the elbow is used to visualize the suspect diagnosis of a fracture. Hence, every child with a traumatic injury to the elbow visiting the ED must endure a very small but potentially harmful dosage of radiation, even though the majority of these patients have no fracture. A decision rule may be useful to reduce the number of unnecessary radiographs.

More than a decade ago, the research group of Appelboam A. et al(2) developed the elbow extension test, a decision rule to enhance selective radiography and decrease the risks of radiation by reducing the number of unnecessary X-rays. The use of this decision rule ultimately led to an absolute reduction in the number of unnecessary plain radiography taken from children. This trend is also seen in other decision rules designed for injuries to other joints, such as the ankle, knee, wrist and neck.(3–7)

Recently, a research group in Amsterdam developed the Amsterdam Pediatric Wrist Rules (APWR) (8,9), the first validated decision rule for pediatric acute wrist trauma. With the implementation of the APWR, an absolute reduction of 19% of the unnecessary radiographs was seen. These data highlight a knowledge gap and opportunity for the development of a decision rule for pediatric elbow fractures.

Our research objective is to develop, validate and implement an extended decision rule for pediatric elbow fractures (the Pediatric Elbow Trauma rules) to improve selective radiographic imaging and reduce unnecessary exposure to radiation in children. Furthermore, we aim to improve the quality of care for children who present at the emergency care with an injury of the elbow by reducing the waiting times and health care costs.

Methods and analysis

Study design

This is a multi-center prospective observational study of pediatric patients who visit the emergency department with a traumatic elbow injury. The data will be collected in four different hospitals; one academic hospital, two large teaching hospitals and one general hospital.

The first part of this research is the development of the decision rule with use of clinical parameters obtained from baseline patient characteristics, patient interview and physical examination. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will determine which clinical parameters provide a possible predictive value for elbow fractures. We will collect all clinical parameters (originating from the expert panel) via the patient history and physical examination from all patients. All patients will get radiographs of the affected elbows and will be provided emergency care according to local

hospital protocols. These patient data will be processed in a multivariable logistic regression analysis to determine the clinical parameters that predict the presence or absence of an elbow fracture. Only the clinical parameters which significantly predict a fracture, within this prediction model, will be used to formulate the new decision rule.

In the second part of this research, the newly developed decision rule will undergo internal validation using the data gathered in the first part of the research. At the same time we will determine the primary outcome measurements: the potential absolute reduction in the number of X-ray examinations, a calculation detailing how much costs have been saved by taking more selective X-rays and a calculation on time saved during an ED visit.

Study population

The study population is defined as all consecutive children/adolescents aged two to seventeen years who visit the emergency department of one of the participating hospitals with pain following elbow trauma. The anatomical region of the elbow is defined as the bony and articular surfaces of the distal humerus, the proximal ulna and the proximal radius.(10) A traumatic injury is defined as any direct or indirect low- or high-energetic trauma involving the elbow. A full list describing the inclusion and exclusion criteria is given in table 1.

Inclusion criteria
- Patients aged between 2 and 17 years
- Traumatic injury of the elbow (maximum 72 hrs prior to presentation on the emergency department
- Pain in the anatomical region of the elbow joint
Exclusion criteria
- Pre-existent neurological pathology, genetic disorders and/or bone disorders in the affected limb
- Current ipsilateral fracture of wrist or shoulder
- Previous fracture of the ipsilateral upper extremity (from clavicle to distal phalanges) <3 months
- Patients referred from another hospital where X- rays of the elbow were performed
- A multitrauma patient (Injury severity score > 16)
- Children with an intellectual disability
- Unable to communicate in Dutch or English

Table 1: Inclusion and exclusion criteria used during the selection of pediatric patients in this study.

Sample size

A traditional sample size calculation is not recommended due to the multivariable character of this study. A sample size calculation through its ability to accurately estimate effect size is chosen, therefore a modified convenience sample will be used. A logistic regression analysis is used to determine the potential variables for the final decision rule. The variance between outcomes per variable within a regression analysis dictates the sample size per variable. The variance between outcomes for the potential variables in the decision rule is estimated to be very small (predominantly yes/no answers). Jenkins et al, Riley et al and Steyerberg et al (11–

13) described a detailed calculation for an adequate sample size in clinical decision/prediction models. Based on their recommendations, we aim to include 400 patients for our study. To summarize: on average 8-12 participants are needed per variable to ensure a valid prediction can be made concerning the variables' discriminative value. To increase the accuracy of the prediction model, we will focus on 10 predictive potential variables with a high a-priori chance of underlying traumatic injury to the bone. Therefore, we will need to include a minimum of 100 patients (10 variables x 10 patients). To ensure an accurate internal validation for our updated clinical decision rule a minimum of 300 patients must be included.(13) Based on these estimates we have chosen to include 400 patients for our research.

Statistical analysis

The data from standardized electronic case report forms (CRFs) will be used to develop the prediction model, by using a multistep logistic multivariable analysis in a shrinkage model. The shrinkage model used will be a ridge regression, because of its ability to analyze data suffering from multicollinearity (multiple independent variables are correlated). During the first step, a univariate logistic regression analysis will be used to estimate the regression coefficients and analyze the correlation between a variable and the presence or absence of a fracture. The regression coefficients will be processed, in the second step, through a multivariate shrinkage model to establish significant regression coefficients and generate a relative risk score per variable. Sensitivity, specificity, positive predictive value and negative predictive values will be gathered. The accuracy of the model will be estimated by a goodness of fit test with a graphical calibration curve and a receiver operating characteristics (ROC) curve with a discriminative curve. Overfitting will be controlled by calculating the optimism estimation of the C-statistic. Internal validation will be performed through bootstrapping to estimate overfitting and adjust the model accordingly. The final decision rule will be presented as a simplified risk score for easy use by emergency care physicians.

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We will use three strategies to avoid or adequately substitute potential missing data: (1) optimizing the study design and implementation methods to avoid missing data, such as; training doctors, creating simplified CRFs and adhering to normal treatment protocol, (2) sending regular updates to all participating hospitals, (3) investigating patterns of missing data to allow analyses to explore potential reasons for missing data and impute missing values by chained equations to avoid bias.

Study procedures

Data collection will take place starting May 2023 and will be completed after including 400 patients, preferably within a 2-year period. All pediatric patients presenting to the emergency department following a traumatic injury of the elbow will receive care as usual according to hospital protocol. To develop the decision rule, we will collect patient characteristics in a standardized fashion during the interview and physical examination. A standardized electronic case report form will be generated to collect the data during the participant's visit. The CRF will contain basis information on patient characteristics such as age, gender, injured arm, it will also include a physical examination, the results of the x-ray and the possible predictive clinical parameters. The attending (orthopedic/surgical) physicians collecting the data will receive instructions and training before recruiting

participants to the study. Possible predictive clinical parameters are patient age and gender, point tenderness at lateral or medial distal humerus, radial head, olecranon, limited range of motion for supination/pronation/flexion and extension, hypoesthesia of the lower arm, increased capillary refill test, visible hematoma and trauma injury mechanism. All participants will receive plain elbow radiographs, according to Dutch guidelines; anterior-posterior view with the hand in anatomical position and a lateral view with the thumb in upwards position.(14) Additional imaging for associated injuries or to confirm suspected diagnosis will be performed at the discretion of the treating orthopedic or trauma physician.

Primary outcome parameters

Our primary outcome measurement is the existence of a fracture on the conventional x-ray diagnosed by a musculoskeletal radiologist. A fracture is defined as a partial or complete disruption of one or more of the cortices in the ulna, radius or humerus within the elbow region and all epiphysial growth plate injuries visible on AP or lateral view. Avulsions or displacement of apophyseal growth plates are also defined as a fracture. All additional imaging (radiography, magnetic resonance imaging or computed tomography) performed by the on-call physician and radiologist will be taken into account when diagnosing the fracture.

Our primary outcome, a fracture of the elbow, will be measured after inclusion of all 400 patients. All participants will receive a conventional radiography. After inclusion has ended all conventional radiographs will be gathered for final inspection. This will be done by two musculoskeletal radiologist in consensual agreement and blinded to the clinical parameters and medical history of the patient. The two musculoskeletal radiologist will provide a detailed diagnostic report, after reaching consensus, for every radiography performed on our patients. This final report will dictate the presence or absence of a fracture of the elbow after traumatic injury to the elbow in the pediatric patient.

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Participants can leave the study at any time for any reason if they wish to do so without any consequences. The principal investigator or treating physician can decide to withdraw a subject from the study for urgent medical reasons.

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who are willing to join will receive similar treatment, the only difference is that clinical parameters recorded during patient interview and physical examination will be more extensive and will be recorded in a case report form.

Patient and public involvement

No patients were involved during the creation of this study protocol.

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Handling and storage of data and documents

All acquired patient-related data will be anonymously coded with a referencing legend for safe used by members of the research team. Research data will be stored in a database (SPSS version 25 and Castor EDC and SMS) and can be traced to individual persons only by authorized personnel. The personnel authorized to view the database include the members of the research team, members of the health care inspection, and members of the Medical Ethics Committee. Review of the data may be necessary to ensure the reliability and quality of the research. The handling of personal data is in compliance with the Dutch act on Implementation of the General Data protection Regulation (in Dutch: 'Wet Algemene Verordening Gegevensbescherming persoonsgegevens'), the EU General Data Protection Regulation and the privacy regulation of all involved hospitals.

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Development and validation of the Pediatric Elbow Trauma (PET) rules as a decision rule for radiography in traumatic elbow injuries: A study protocol

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Development and validation of the Pediatric Elbow Trauma (PET) rules as a decision rule for radiography in traumatic elbow injuries: A study protocol

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In the process of creating the manuscript, the seven authors fulfilled the following roles and tasks:

1. TFF *Main author*; setup the design of the study, recruiting an expert panel, conception and writing of the manuscript
2. CJA *Study designer*; conception and design of the study, provided orthopedic and scientific expertise and critical revisions to the study protocol.
3. B *Expert panel*; providing critical revisions and help with interpretation of data
4. PBH *Expert panel*; providing critical revisions and help with interpretation of data
5. NWL *Expert panel*; providing critical revisions and help with interpretation of data
6. LC *Legal counsel and statistical help*; aided in legal issues, assisted with administration and data management, provided statistical help.
7. D *Final* author; conception and design of the study, provided orthopedic and scientific expertise and critical revisions to the study protocol. Final author of the manuscript.

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None.

Abstract

Background: Traumatic elbow injuries in children occur frequently and are among the most common traumatic injuries seen on the Emergency Department (ED) and in general practice. The use of a validated decision rule to enhance selective radiography in pediatric patients with possible elbow fractures may reduce unnecessary exposure to radiation in children.

Method and analysis: This study is designed as a multicenter prospective cohort study. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will initially determine clinical parameters that provide a possible predictive value for elbow fractures. Four hundred children between the ages of 2 and 17 years visiting the ED with pain following elbow trauma will then be included. The clinical parameters will be collected via patient history and physical examination. Elbow radiographs will be obtained in all patients to identify fractures. The data will be processed in a multivariable logistic regression analysis to determine which clinical parameters predict the presence of an elbow fracture. Only the clinical parameters that predict a fracture will be used to formulate the new decision rule: the pediatric elbow trauma (PET) rules. Internal validation of the prediction model will take place after inclusion is complete and by means of a bootstrap analysis on the acquired data. A calculation will be made to determine how many radiographs can potentially be reduced by applying the PET-rules and a cost-analysis will be performed.

Ethics and dissemination

The study will be conducted according to the principles of the Declaration of Helsinki and in accordance with the Medical Research Involving Human Subjects Act. The Medical Research Ethics Committees United stated on 16 may 2022 that The Medical Research Involving Human Act (WMO) does not apply to this study and an official approval by the committee is not required, reference number; project W22.086.

SUMMARY

What is known about the subject?

Pediatric elbow fractures are very common and only one diagnostic decision rule is available. Every child will have undergone a plain radiography to check for possible fractures.

What this study hopes to add?

To modernize the diagnostic decision rule for pediatric elbow fracture and increase its sensitivity and to reduce the unnecessary radiation exposure to children on the emergency care when taking an overabundant radiography.

How this study might affect research, practice and policy?

To ensure not every child undergoes a radiography, but only those with a high chance of elbow fracture decided through our decision rule.

Introduction

Elbow fractures are defined as fracture of the distal part of the humerus and/or proximal part of the radius and/or proximal part of the ulna. Forty percent to 60% of all boys and 25% to 40% of all girls will visit the emergency care with a fracture during their childhood.(1) Pediatric elbow fractures are amongst the most common injuries seen on the ED(1). Incorrect diagnosis and treatment can lead to undesirable pain and decreased range of motion during adult life.

Plain radiography of the elbow is used to visualize the suspect diagnosis of a fracture. In the Netherlands, every child with a traumatic injury to the elbow visiting the ED must endure this very small but potentially harmful dosage of radiation, even though the majority of these patients have no fracture.(2) A decision rule may be useful to reduce the number of unnecessary radiographs.

More than a decade ago, the research group of Appelboam A. et al(3) developed the elbow extension test, a decision rule to enhance selective radiography and decrease the risks of radiation by reducing the number of unnecessary X-rays. The use of this decision rule ultimately led to an absolute reduction in the number of unnecessary plain radiography taken from children. This trend is also seen in other decision rules designed for injuries to other joints, such as the ankle, knee, wrist and neck.(4–8)

Recently, a research group in Amsterdam developed the Amsterdam Pediatric Wrist Rules (APWR) (9,10), the first validated decision rule for pediatric acute wrist trauma. With the implementation of the APWR, an absolute reduction of 19% of the unnecessary radiographs was seen. These data highlight a knowledge gap and opportunity for the development of a decision rule for pediatric elbow fractures.

Our research objective is to develop and validate an extended decision rule for pediatric elbow fractures (the Pediatric Elbow Trauma rules) to improve selective radiographic imaging.. Furthermore, we aim to improve the quality of care for children who present at the emergency care with an injury of the elbow by reducing the waiting times and health care costs.

Methods and analysis

Study design

This is a multi-center prospective observational study of pediatric patients who visit the emergency department with a traumatic elbow injury. The data will be collected in four different hospitals; one academic hospital, two large teaching hospitals and one general hospital.

The first part of this research is the development of the decision rule with use of clinical parameters obtained from baseline patient characteristics, patient interview and physical examination. An expert panel of orthopedic elbow surgeons, pediatric orthopedic surgeons and trauma surgeons will determine which clinical parameters provide a possible predictive value for elbow fractures. We will collect all clinical parameters (originating from the expert panel) via the patient history and physical examination from all patients. All patients will get radiographs of the affected elbows and will be provided emergency care according to local

hospital protocols. These patient data will be processed in a multivariable logistic regression analysis to determine the clinical parameters that predict the presence or absence of an elbow fracture. Only the clinical parameters which significantly predict a fracture, within this prediction model, will be used to formulate the new decision rule.

In the second part of this research, the newly developed decision rule will undergo internal validation using separate data identically gathered in a prospective fashion. At the same time we will determine the primary outcome measurements: the potential absolute reduction in the number of X-ray examinations, a calculation detailing how much costs have been saved by taking more selective X-rays and a calculation on time saved during an ED visit.

The final study will include a completed version of the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) checklist. With this checklist we hope to improve the transparency of our research by identifying the important factors in the prognostic prediction model, according to the TRIPOD statement.

Study population

The study population is defined as all consecutive children/adolescents aged two to seventeen years who visit the emergency department of one of the participating hospitals with pain following elbow trauma. The anatomical region of the elbow is defined as the bony and articular surfaces of the distal humerus, the proximal ulna and the proximal radius.(11) A traumatic injury is defined as any direct or indirect low- or high-energetic trauma involving the elbow. A full list describing the inclusion and exclusion criteria is given in table 1.

Inclusion criteria	
	- Patients aged between 2 and 17 years
	- Traumatic injury of the elbow (maximum 72 hrs prior to presentation on the emergency department
	- Pain in the anatomical region of the elbow joint

Exclusion criteria	
	- Pre-existent neurological pathology, genetic disorders and/or bone disorders in the affected limb
	- Current ipsilateral fracture of wrist or shoulder
	- Previous fracture of the ipsilateral upper extremity (from clavicle to distal phalanges) <3 months
	- Patients referred from another hospital where X- rays of the elbow were performed
	- A multitrauma patient (Injury severity score > 16)
	- Children with an intellectual disability
	- Unable to communicate in Dutch or English

Table 1: Inclusion and exclusion criteria used during the selection of pediatric patients in this study.

Sample size

A traditional sample size calculation is not recommended due to the multivariable character of this study. A sample size calculation through its ability to accurately estimate effect size is chosen, therefore a modified convenience sample will be used. A logistic regression analysis is used to determine the potential variables for the final decision rule. The variance between outcomes per variable within a regression analysis dictates the sample size per variable. The variance between outcomes for the potential variables in the decision rule is estimated to be very small (predominantly yes/no answers). Jenkins et al, Riley et al and Steyerberg et al (12–14) described a detailed calculation for an adequate sample size in clinical decision/prediction models. Based on their recommendations, we aim to include 400 patients for our study. To summarize: on average 8-12 participants are needed per variable to ensure a valid prediction can be made concerning the variables' discriminative value. To increase the accuracy of the prediction model, we will focus on 10 predictive potential variables with a high a-priori chance of underlying traumatic injury to the bone. Therefore, we will need to include a minimum of 100 patients (10 variables x 10 patients). To ensure an accurate internal validation for our updated clinical decision rule a minimum of 300 patients must be included.(14) Based on these estimates we have chosen to include 400 patients for our research; 100 patients (25%) for the development of the decision rule and 300 patients (75%) for the internal validation of the decision rule

Statistical analysis

The data from standardized electronic case report forms (CRFs) will be used to develop the prediction model, by using a multistep logistic multivariable analysis in a shrinkage model. The shrinkage model used will be a ridge regression, because of its ability to analyze data suffering from multicollinearity (multiple independent variables are correlated). During the first step, a univariate logistic regression analysis will be used to estimate the regression coefficients and analyze the correlation between a variable and the presence or absence of a fracture. The regression coefficients will be processed, in the second step, through a multivariate shrinkage model to establish significant regression coefficients and generate a relative risk score per variable. Sensitivity, specificity, positive predictive value and negative predictive values will be gathered. The accuracy of the model will be estimated by a goodness of fit test with a graphical calibration curve and a receiver operating characteristics (ROC) curve with a discriminative curve. Overfitting will be controlled by calculating the optimism estimation of the C-statistic. Internal validation will be performed through bootstrapping to estimate overfitting and adjust the model accordingly. The final decision rule will be presented as a simplified risk score for easy use by emergency care physicians.

Missing data

We will use three strategies to avoid or adequately substitute potential missing data: (1) optimizing the study design and implementation methods to avoid missing data, such as; training doctors, creating simplified CRFs and adhering to normal treatment protocol, (2) sending regular updates to all participating hospitals, (3) investigating patterns of missing data to allow analyses to explore potential reasons for missing data and impute missing values by chained equations to avoid bias.

Study procedures

Data collection will take place starting May 2023 and will be completed after including 400 patients, preferably within a 2-year period. All pediatric patients presenting to the

emergency department following a traumatic injury of the elbow will receive care as usual according to hospital protocol. To develop the decision rule, we will collect patient characteristics in a standardized fashion during the interview and physical examination. A standardized electronic case report form will be generated to collect the data during the participant's visit. The CRF will contain basis information on patient characteristics such as age, gender, injured arm, it will also include a physical examination, the results of the x-ray and the possible predictive clinical parameters. The attending (orthopedic/surgical) physicians collecting the data will receive instructions and training before recruiting participants to the study. Possible predictive clinical parameters are patient age and gender, point tenderness at lateral or medial distal humerus, radial head, olecranon, limited range of motion for supination/pronation/flexion and extension, hypoesthesia of the lower arm, increased capillary refill test, visible hematoma and trauma injury mechanism. All participants will receive plain elbow radiographs, according to Dutch guidelines; anterior-posterior view with the hand in anatomical position and a lateral view with the thumb in upwards position.(15) Additional imaging for associated injuries or to confirm suspected diagnosis will be performed at the discretion of the treating orthopedic or trauma physician.

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