Establishing routine preoperative gastric ultrasound for patients with an increased aspiration risk in a Swiss teaching hospital: A prospective observational study.

Project Category: Observational Study - Risk category A

Project Short Title: Gastric sonography before anaesthesia inductions

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Project Plan Version number und Date:	Version 3.0 – 25.01.2021
Project Identifier:	2020-02858
Category	HFV Project Category A

Synopsis

Sponsor	Prof. med. Michael T. Ganter
Principal investigator	Dr. med. Roman Meierhans
Study Title:	Establishing routine preoperativ gastric ultrasound for patients with an increased aspiration risk in a Swiss teaching hospital: A prospective observational study
Short Title / Study ID:	Establishing gastric sonography in a Swiss teaching hospital 2020-02858
Protocol Version and Date:	V3.0 – 25.01.2021
Trial registration:	Clinical Trials.gov: to be determined
Study category and Rationale	HFV Project - Category A Gastric sonography is a low risk examination. No ionizing radiation is used. Theoretical complications including sensation of local pressure or pain, regional exanthema or allergic reactions to ultrasonic gel will at most be very minor. The complete examination takes approximately five minutes, accordingly anaesthesiologic and surgical procedures will not be significantly delayed. Patients and interventions where even a minimal delay may provide a potential health risk are not included in this study.
Background and Rationale:	Aspiration pneumonias still exhibit a significant morbidity and mortality[1-6] and are accountable for a significant part of anaesthesia-related deaths. Various diseases and especially emergency situations correlate with prolonged gastric emptying and therefore with a higher risk of pulmonary aspiration. In clinical practice the decision to perform a Rapid Sequence Induction (RSI) is mostly based on clinical and anamnestic findings. Preoperative gastric sonography may provide an objective, validated, non-invasive, reliable, fast, and cost-efficient approach to assess aspiration risks in both elective and emergency patients. How this highly sensitive and specific tool may be best introduced and implemented in daily clinical practice or anaesthesiologic guidelines remains unclear. Structured educational programmes or training recommendations for this point-of-care ultrasound application rarely exist.
Objectives:	1. Establish preoperative gastric sonography before Rapid Sequence Induction (RSI) and patients with one or more aspiration risk factors scheduled for a advanced laryngeal mask or regional anaesthesia at the Kantonsspital Winterthur, Department of Anaesthesiology. 2. Validation of our structured training/education by comparing sonographic estimated and directly measured gastric content. 3. Emphasize the importance and effectiveness of this diagnostic tool to improve anaesthesiologic management.

Outcomes:	**Primary Endpoint:** - Correlation of sonographic estimated gastric volume with volume aspirated through a naso- or orogastric tube. **Secondary Endpoints:** - Performance over time, improvement of examination technique, critical number of examinations to achieve a high quality standard (>80% congruece for estimated and aspirated gastric volume in fluids). - Association of performance with experience, residents vs. attendings. - Number of patients classified as empty -> possible implications for management and induction - Number of patients with full stomach -> possible implications for management and induction - Time used for examinations, time used with growing experience. - estimated aspiration risk vs. sonographic gastric volume - Total number of pulmonary aspirations
Study design	A prospective observational study
Inclusion criteria:	• All elective in-hospital Rapid Sequence Inductions (RSI) and patients with one or more aspiration risk factors scheduled for a advanced laryngeal mask or regional anaesthesia with informed consent. • All emergency in-hospital RSI and patients with one or more aspiration risk factors scheduled for an advanced laryngeal mask or regional anaesthesia with informed consent graded as follows according to the Swiss Society for Anaesthesiology and Resuscitation (A-QUA): “Notfall 1-6h, nicht vital (dringlicher Eingriff)”, “Notfall 6-24h nicht vital (aufgeschobener dringlicher Eingriff)”
Exclusion criteria:	• Life threatening/ time critical emergency interventions, graded followingly according to the Swiss Society for Anaesthesiology and Resuscitation (A-QUA): “Notfall <1h, vital (sofortiger Eingriff notwendig)” • Known Pregnancy • Obstetric surgery • Underage (< 18 years) • Absence of informed consent (missing or inability to provide) • No anaesthetist with completed structural education in gastric sonography is available. • Contraindications for naso- or orogastric tubes or inability to correctly place such.
Intervention, Measurements and procedures:	Our study will be performed mainly in the induction rooms of our operating ward and occasionally inside the operating theatre. Standard care will be given to every patient at the usual location, with our usual equipment (anaesthetic machine, monitoring, medication and airway devices etc) and by our usual anaesthesiologic team members. Sonographic examination and determination of the gastric content will be executed on one of our standard ultrasound machines (Venue and LOQIC e from GE-Healthcare®) with a curved

	array low frequency (2-10 Hz) abdominal probe or portable ultrasound devices (IQ+ from Butterfly Network Inc. ®).
Control Intervention:	
Number of Participants with Rationale:	A total number of 2'718 general anaesthesia with Rapid Sequence Inductions (RSI) was undertaken at our institution in 2019. Thereof, 275 were children < 18 years of age. 204 Rapid Sequence Inductions were performed in category: "Notfall <1h, vital, sofortiger Eingriff notwendig" and therefore not includable. Therefore, expect to include around 1500 - 2200 patients in a one year period.
Study Duration:	Estimated duration of the project: 18 months Planned start: 01/2021 Planned project close: 06/2022
Study Schedule:	Project specific: • Time period for participant recruitment: 12 months Project start (FPFV): 01/2021 • Project end (LPLV): 12/2021
Investigators:	Michael T. Ganter (Sponsor), Roman Meierhans (PI) Co-Investigators: Sascha J. Baettig, Mark G Filipovic, Daniela Widmer Sub-Investigators: All anaesthesia faculties and residents of the department of Anaesthesiology, Kantonsspital Winterthur after completion of our special training program in gastric sonography (see Chapter 8) All investigators are members of: Department of Anaesthesiology Kantonsspital Winterthur Brauerstrasse 15 8400 Winterthur, Switzerland
Study Centre:	This study will be conducted at the Department of Anaesthesiology at the Cantonal Hospital of Winterthur, a Swiss teaching hospital. In our department we care for a total of approximately 18'000 patients per year. The anaesthetic physician team consists of 25 qualified/staff anaesthetists and 29 trainee anaesthetists, all with basic knowledge of point-of-care-ultrasound (e.g. vascular access, peripheral nerve blocks). In the past several clinical studies including multi- as well as single-centre studies have been successfully conducted at our institution.
Statistical Considerations:	Collected Variables • Patient Demographic: Age, sex, gender, height, weight, BMI, ASA Classification, patient history, concomittant medication, concomitant disease, intervention performed, anaesthetic risk class of the intervention, surgical department of the intervention, urgency of the intervention. • Sonographer Demographic: education level, years of anaestesiologic experience, years of sonographic experience

	• risk factors for pulmonary aspiration • Last meal/ drink before surgery • Subjective estimated aspiration risk (graded by the responsible anaesthetist) • Sonography quality, reasons for poor quality • Sonographic quality of gastric content • Sonographic quantity of gastric content • Time for examination • Effective quantity of gastric content • Theoretical change in anaesthesiologic management • Reason for not performing gastric sonography Analyses • Institution overall success analysis • Interpersonal success analysis • Analysis of theoretical changes in anaesthesiologic management
GCP Statement:	This study will be conducted in compliance with the study protocol, the current version of the Declaration of Helsinki, the ICH-GCP directive, the HFG and HFV as well as all other relevant national legal and regulatory requirements.

Study Schedule

	Expert and Resident Training in Sonography (11/2020 – 02/2021)	**Screening (01/2021 – 12/2021)** **Prior to arrival at OR suite**	**Day of Surgery (01/2021 – 12/2021)** **= Day 1**
Expert (study core group, faculties) Training	√		
Anaesthesia resident Training	√		
Training Participants Demographic and Experience Data	√		
Participant Information and Informed Consent		√	
Inclusion- and Exclusion Criteria		√	
Demographic Data		√	
Medical History / Concomitant Diseases / Concomitant Medication		√	
Sonography and Data Collection			√
Gastric Volume direct measurement			√
Serious Events			√

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1 Abbreviations

HFG	Humanforschungsgesetz
HFV	Humanforschungsverordnung (Ordinance on human research with exception of clinical trials/HRO)
HRO	Human Research Ordinance
ICH	International Conference on Harmonization
SE	Serious Event
RSI	Rapid Sequence Induction
POCUS	Point-of-care ultrasound
CSA	Cross sectional area
SGAR	Swiss Society for Anaesthesiology and Resuscitation

2 Project Personal and Administration

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Co-Investigators:	Dr. med. Sascha J. Bättig Department of Anaesthesiology Kantonsspital Winterthur Brauerstrasse 15 8400 Winterthur, Switzerland +41 (0)52 266 38 06 sascha.baettig@ksw.ch Dr. med. Mark G. Filipovic Department of Anaesthesiology Kantonsspital Winterthur Brauerstrasse 15 8400 Winterthur, Switzerland +41 (0)52 266 49 88 mark.filipovic@ksw.ch Daniela Widmer Department of Anaesthesiology Kantonsspital Winterthur Brauerstrasse 15 8400 Winterthur, Switzerland +41 (0)52 266 27 92 daniela.widmer@ksw.ch
Biostatistician:	To be determined

3 Introduction

This project plan describes the conduction of a scientific research project according HFV category A - the collection of health related personal data with minimal risks and burdens.

Aspiration pneumonias still exhibit a substantial morbidity and mortality[1-6] and are accountable for a significant part of anaesthesia-related deaths.[6, 7] Various diseases and especially emergency situations correlate with prolonged gastric emptying and therefore with a higher risk of pulmonary aspiration. [1, 4] To minimize the risk of aspiration, Rapid Sequence Induction (RSI) with subsequent routine placement of a oro- or nasogastric tube is recognized as the anaesthesiologic procedure of choice in these situations. [16] In clinical practice the decision to perform a RSI is mostly based on clinical and anamnestic findings. In contrast, preoperative gastric sonography may provide an objective, validated, non-invasive, reliable, fast, and cost-efficient approach to assess aspiration risks in both elective and emergency patients.

How this highly sensitive and specific tool may be best introduced and implemented in daily clinical practice or anaesthesiologic guidelines remains unclear. Structured educational programmes or training recommendations for this point-of-care ultrasound application rarely exist. We aim to investigate the implementation of such a structured learning program in a teaching hospital, validating it's effectiveness and thus lay ground to improve anaesthesiologic management and patient safety.

3.1 Background and Project Purpose

In 1946, Mendelson[8] was first to recognize the potential danger of anaesthesia related pulmonary aspiration, defined as the presence of bilious secretion in the tracheobronchial tree, and to describe its detrimental consequences.[1] The presence of intestinal fluids in the respiratory system results in a chemical pneumonitis and may lead to acute hypoxemia or bronchospasm or end up in an aspiration pneumonia.[9] Pulmonary aspiration is a relatively rare event, with an incidence ranging from 0.01 up to 0.8 % according to literature.[1-5, 10] Despite its low incidence, aspiration pneumonias may still exhibit a substantial morbidity and mortality[1-6] and are accountable for a significant part of anaesthesia-related deaths.[6, 7]

The majority of the perioperative pulmonary aspirations occur shortly before or during laryngoscopy or throughout extubation.[1, 6] In emergency or critical care medicine the risk of pulmonary aspiration seems to be significantly increased.[10, 11] Further risk factors include gastrointestinal obstruction, recent food intake, lack of coordination of swallowing, obesity, ASA status, pregnancy, age, surgical procedure and other co-morbidities (insulin dependent diabetes, hepatobiliary- or renal dysfunction or cardiorespiratory diseases).[1, 4]

Accordingly, strategies to reduce the risk of aspiration have been developed and continuously updated. For elective surgeries American[12] and European[13] guidelines recommend a minimum fasting time of 6 hours for solid an 2 hours for clear fluids. Recent guideline updates for paediatric patients resulted in a reduced fasting time for clear liquids of 1 hour prior to elective surgery, as prolonged fasting times had been identified as a negative predictor for adverse physiological response to surgery and reduced fasting intervals improved patient comfort and compliance.[14, 15]

For emergency surgeries in non-fasten patients or patients with increased risk of aspiration Rapid Sequence Induction (RSI) is broadly accepted and executed as a standard procedure.[16] However, RSI is accompanied by significant risks concerning haemodynamic stability and oxygenation in case intubation and mask ventilation fails. [17, 18] Most importantly, evidence of a decreased incidence of pulmonary aspiration after Rapid Sequence Induction (RSI) is still lacking.[19]

Fast, simple, non-invasive and cost-effective strategies to assess a patient's risk of aspiration and adapt the anaesthetic strategy accordingly are greatly needed. Here, point-of-care sonography (POCUS) with preoperative assessment of the gastric content allows a fundamentally new approach for patients at risk of gastric regurgitation by adding an objective tool - not relying on patient history alone.[11, 20] Gastric sonography seems to be highly sensitive and specific.[21, 22] Recent studies, especially highlighted the accuracy for the qualitative[23-27] and quantitative assessment[22, 25, 26, 28] of the gastric content. For the quantitative analysis of gastric content, present data suggest a strong numerical correlation between an ultrasound-determined antral cross-sectional area (CSA) and the total volume of gastric fluid.[11, 28] A residual gastric volume of more than 1.5 ml/kg for fluid content has been identified to signal an increased risk for gastrointestinal regurgitation and for pulmonary aspiration and this cut-off value has been utilized in various studies.[20, 29] Consequently, there is an increasing consensus in scientific literature that preoperative gastric sonography should be performed in all emergency situations and in elective interventions in patients with increased probability of presenting with a full stomach and accordingly an increased risk of pulmonary aspiration.[30-34] The routine application of gastric POCUS for elective surgery with fasted patients without risk factors is still controversial[11] although Van de Putte et al.[35] discovered a relevant percentage of full-stomachs in patients without risk factors of delayed emptying of the stomach.

In summary, preoperative gastric sonography may provide a validated, reliable, fast, and cost-efficient approach to assess aspiration risks in both elective and emergency patients. Practiced sonographers are able to perform point-of-care gastric sonography in few minutes[11, 27] , thus severe delay in daily clinical practice should not be expected. Nevertheless, how this highly sensitive and specific tool should be best established in daily clinical practice is further on unclear. There is no existing structural education/training for this specific point-of-care ultrasound application. Arzola et al. suggest a minimum of 30 ultrasounds an acceptable quality level, but evidence is scarce.[36]

The aim of this investigation is to validate our structural training and proof the importance and effectiveness of this diagnostic tool to lay ground for improvement of anaesthesiologic management and presumably patient safety in patients with an increased risk of a pulmonary aspiration.

3.2 Categorisation

Category A: collection of health related personal data is associated with minimal risk and burdens only.

Gastric sonography is a very low risk examination. No ionizing radiation is used. Theoretical complications including sensation of local pressure or pain, regional exanthema or allergic reactions to ultrasonic gel will at most be very minor. The complete examination takes approximately five minutes accordingly anaesthesiologic and surgical procedures will not be significantly delayed. Patients and inteventions where even a minimal delay may pro-vide a potential health risk are not included in this study.

4 Project Objectives

4.1 Project Objectives

Primary objectives:

- Establish preoperative gastric sonography in patients with risk factors for pulmonary aspiration at the Kantonsspital Winterthur, Department of Anaesthesiology through a structured training/education - validated by comparing sonographic estimated and directly measured gastric content.

Secondary objectives:

- Identify possible confounders and variables in individual training.
- Emphasize the importance and effectiveness of this diagnostic tool to improve anaesthesiologic management and possibly patient safety by identifying the number of possible interventions and changes in anaesthesiologic management and correlation of estimated and actual gastric volume in fluids.

4.2 Project Outcomes

Primary Endpoint:

- Correlation of sonographic estimated gastric volume with volume aspirated through a naso- or oro-gastric tube, that was placed by routine.

Secondary Endpoints:

- Performance over time, improvement of examination technique, critical number of examinations to achieve a high quality standard (>80% congruece for estimated and aspirated gastric volume in fluids).
- Association of performance with experience, residents vs. attendings.
- Number of patients classified as empty -> possible implications for management and induction.
- Number of patients with full stomach -> possible implications for management and induction.
- Time used for examinations, time used with growing experience.
- Estimated aspiration risk vs. sonographic gastric volume.
- Total number of pulmonary aspirations.

5 Project Description

5.1 Design

Single center, prospective observational study. No intervention groups, one single cohort.

5.2 Number of Project Participants

We aim to include at least 500 up to 2200 patients. For further informations see below.

5.3 Project Schedule

Estimated duration of the project:	18 months
Time period for participant recruitment:	12 months
Project start (FPFV):	01/2021
Project end (LPLV):	12/2021

5.4 Risk-benefit considerations

Gastric sonography is as an accuratly investigated and validated tool to assess a patients fasting status and thus probably aspiration risk. Some authors recently highlighted its possible impact on anaesthesiologic management in finding an appropriate technique for individual patients and thus balance risks and benefits. Nevertheless, gastric sonography has not yet found its role in clinical practice. This prospective observational-study with its large sample size and thorough analysis may help to identify crucial determinants and possible obstacals in establishing gastric sonography in daily practice and may thus contribute to patient safety. Further, participating medical staff benefit from a structured education in performing this examination with high precision and quality.

With this study being oberservational, non interventional, all patients receive the standard of care in form of a predefined, independent anaesthesiologic treatment and do not carry additional risks besides possible side effects due to gastric sonography itself, which are minimal. The possible delay in the anaesthesiologic management ist at maximum a few minutes and patients with time critical interventions will be thoroughly excluded. In exceptional cases the responsible anaesthesiologist is allowed to upgrade patients from an advanced laryngeal mask to a RSI (gold standard) after ultrasound performance to ensure patient safety. Downgrading from RSI to advanced laryngeal maks on base of the ultrasound results is not allowed.

6 Eligibility of the Project Site

This study will be conducted at the Department of Anaesthesiology at the Cantonal Hospital of Winterthur, a Swiss teaching hospital. In our department we care for a total of approximately 18’000 patients a year. The anaesthesiologic physician team consists of 25 qualified/staff anaesthetists and 29 trainee anaesthetists. In the past several clinical studies including multi- as well as single-center studies have been successfully conducted at our institution. Commulative experience of the assigned staff are high: They have participated in several observational studies as well as interventional studies and Phase III trials. An experienced study coordination team is available at site and involved in coordination and planning.

7 Recruitment

Within a study period of 6 to 12 months, all elective and emergency patients with one or more risk factors for pulmonary aspiratipon will be screend for possible participation in this study. The risk factors for pulmonary aspiration are previously determined by the responsible anaesthetist and based on patient medical history and clinical findings according to department standards. With the given information and in line with department policy, the responsible anaesthesiologist will predefine an individual management for the patient, in form of an advanced laryngeal mask, a RSI or a regional anaesthesia. No changes in or adaptions of the established clinical practice will be made for the sole purpose of this study.

The responsible anaesthesiologist will work through the list of inclusion and exclusion criteria. Of note, patients which are of the highest urgency where a delay is medically and ethically not acceptable, will not be included in this study. Also, patients where ability to consent is not given due to patient or circumstantial reasons, will be excluded.

Thereafter, further recruitment and informed consent will be obtained during a regular anaesthesia specific discussion, which can take place on the ward, in our preoperative consultation for elective surgery or the emergency department. If a patient qualifies for this study according to our inclusion criterias, a qualified studyperson will explain the nature of the study to each participant, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail, according to good clinical practice guidelines. Members of the department of anaesthesia will receive a training by the PI and investigators prior to appointment as qualified studyperson with delegated informed consent authorization. Each participant will be informed that the participation in the study is voluntary and that he/she may withdraw from the study at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment.

After the discussion, an additional information brochure and consent form will be handed to all possible participants providing sufficient information to make an informed decision. The patient will be asked to carefully read and review the form, clarify possible questions at any time and sufficient time will be provided before signing. After the participants signature, the form will also be dated and signed by the study person and retained as part of the study records. If the patient needs further time for consideration the patient may sign the informed consent togheter with the responsible anaesthesist on the day of surgery, after a overnight reflection period. If unanswered questions arise or the patient need further clarifications a special appointment with a physican of the study team is available anytime. The participant will receive a copy of the signed informed consent.

The participant will be informed that his/her medical records may be examined by authorised individuals other than their treating physician.

7.1 Inclusion Criteria

Subjects, who will fulfil all the following inclusion criteria, may be included into this project:

- All elective in-hospital Rapid Sequence Inductions (RSI) and patients with one or more aspiration risk factors scheduled for an advanced laryngeal mask or regional anaesthesia with informed consent.

- All emergency in-hospital RSI and patients with one or more aspiration risk factors scheduled for an advanced laryngeal mask or regional anaesthesia with informed consent graded as follows according to the Swiss Society for Anaesthesiology and Resuscitation (A-QUA): “Notfall 1-6h, nicht vital (dringlicher Eingriff)”, “Notfall 6-24h nicht vital (aufgeschobener dringlicher Eingriff)”

7.2 Exclusion Criteria

If a subject fulfils any of the following exclusion criteria he/she may not be included:

- Life threatening/ time critical emergency interventions, graded followingly according to the Swiss Society for Anaesthesiology and Resuscitation (A-QUA): Notfall <1h, vital (sofortiger Eingriff notwendig)
- Known pregnancy
- Obstetric surgery
- Underage (< 18 years)
- Absence of informed consent (missing or inability to provide)
- No anaesthetist with completed structural education is available.
- Contraindications for naso- or orogastric tubes or inability to correctly place such.

7.3 Premature Withdrawal Criteria

Premature withdrawal of a participant:

- Participants may withdrawal their informed consent at anytime. If gastric sonography has already been performed, anonymous analysis of the previously collected data is eligible.
- Discomfort of pain experienced by the patient at any time of the sonography.
- In case of unability to safely perform the sonography within a maximum of 10 minutes, futher attempts will be stopped and the patient excluded.
- Arising medical or personal information at any time, increasing the urgency of the intervention.

Premature termination of the project:

As this study is designed in a observational, non-interventional methodology, and all patients receive the standard of treatment , no premature termination should occur.

8 Project Measures

8.1 Measures/procedures to collect health related personal data

At Kantosspital Winterthur, a mid-size Swiss teaching hospital all residents and attending anaesthesiologists will receive a structured training in a period of 1 to 8 weeks before inclusion of the first patient. All participating staff will give written informed consent to participate in the study.

To achieve a 90% success rate in correctly recognizing gastric content quality in healthy volunteers, Arzola et al.[36] postulated an average number of 24 sonographic examinations to be performed. Based on this and further scientific studies we designed a structured training for all residents and fellows. Primarily, at least 120 minutes of self-study is mandatory for all participants, consisting of scientific background literature, a step for step guide and educational videos. This is followed by a hands-on course, split into a 30 minute lecture and theoretic background introduction and 120 minutes supervised practical training on healthy volunteers. Group sizes per ultrasound machine and tutor/expert will range from 2 to 3 participants. First training objective is a successful differentiation of gastric content into empty, fluid, solid or mixed. An empty stomach seems the hardest quality to sonographically visualise, [36] therefore a special effort will be made on identifying this quality. The next objective is the identification and localization of the antral cross-sectional area in a supine and right lateral decubitus (RLD) position in the case that fluid gastric content is present. Every participant will perform at least 20 examinations during this hands-on course with a direct expert feedback.

Further, all participants will continue to train their sonographic skills on healthy volunteers and team members at our institution. Before including the first patient all the examiners will be tested by a tutor/expert and received their approval. In the first month of recruitment, new sonographers will be supervised by our tutor/expert team whenever possible. Individual feedback and support if needed should be available any time.

Tutors/experts are all expert sonographers on different modalities. They will receive a preceding 240 minutes training, consisting of a 60 minutes theoretic introduction and a 60 minutes course by a radiologist and abdominal sonography expert, certified by the Swiss Society for Sonography. The remaining time will consist of individual exercise on healthy volunteers and at least 10 trial sonographies with gastric volume calculation under supervision of another member of the tutor group.

Our study will be performed mainly in the induction rooms of our operating unit and occasionally inside the operating theatre. Standard care will be given to every patient at the usual location, with our usual equipment (anaesthetic machine, monitoring, medication and airway devices and so on) and by our usual anaesthesiologic team members. Sonographic examination and determination of the gastric content will be executed on one of our standard ultrasound machines (Venue and LOQIC e from GE-Healthcare®) with a curved array low frequency (2-10 Hz) abdominal probe or our portable ultrasound devices (IQ+ from Butterfly Network Inc. ®).

Before performing the sonographic examination, the responsible anaesthesiologist will be asked to rate the estimated risk of pulmonary aspiration, based on personal impression, patient history and clinical finding. All anaesthetists are advised to perform the examination only if they could guarantee privacy before they expose patient abdomen for the examination. Primary, a qualitative assessment of the gastric content should be performed in supine and right-lateral decubitus (RLD) position. In low volume states a right-lateral decubitus position (RLD) has the advantage of a gravitational shift to the antrum. That is why we plan to perform the examination in both positions. If RLD position is not possible due to patient factors a half sitting position can be tried. Gastric content will be classified into empty, fluid, solid or mixed. Examiners will be asked to classify sonographic conditions into poor, medium or good and provide a reason in case of limited conditions. If fluid gastric content is detected an estimation of the quantity should be performed as follows.

After identification, CSA will be measured and gastric content is estimated by implementation of the formula described by Perlas et al: [20, 28]

Gastric Volume (ml) = 27.0 + 14.6 × right-lateral CSA (cm^2) − 1.28 × age (years).

This model is based on gastroscopic fluid assessment and highly validated by several publications. [28]

After placement of the routine naso- or orogastric tube, which is a standard procedure for both RSIs and advanced laryngeal masksat our institution - we compare the calculated and effective suctioned volume of the gastric content and analyse the difference and quality of the sonographic measurement. In some patient a gastric tube is contraindicated or not possible to place correctly. In this case an exclusion of the study is mandatory according to our exclusion criteria. Patients planed for an intervention in a regional anaesthesia will not receive a gastric tube.

In exceptional cases the responsible anaesthesiologist is allowed to upgrade patients from an advanced laryngeal mask to an RSI after ultrasound performance to ensure patient safety. Downgrading from RSI to advanced laryngeal maks on base of the ultrasound results is not allowed.

All data concerning the sonography will be noted in a password protected Excel sheet only available to institute members by the responsible anaesthesiologist performing the excamination. Background patient data including demographic data are collected during the structured preoperative anaesthesiologic assessment according to in house standard procedures and data management. Data will be coded and condensed in a password-protected Excel File, only accessible to study personel. A patient identification log will be kept in a locked archive for data verification processes only. To guarantee seamless traceability we will create a immutable PDF file after all relevant changes or at least once per month and store it in a separate study folder only accessible to study personel. An additional hard copy will be created and printed once per month and stored in a locker in our administrative office.

9 Safety

9.1 Definition Serious Events

A **serious event (SE)** according to HFV Art. 21 is any unfavorable event for which a causal relationship the collection of health related personal data cannot be ruled out, and which:

- Requires hospitalization or prolongation of an inpatients' hospitalization,
- results in persistent or significant disability or incapacity, oris life-threatening or results in death

If a serious event occurs the research project must to be set on hold.

9.2 Assessment and Documentation of SEs

The assessment by the project leader regarding the causal relationship of the event to the project-specific measure is done according to the following definitions:

Unrelated	• The event started in no temporal relationship to the project-specific measures applied and • The event can be definitely explained by underlying diseases or other situations.
Related	• The event started in plausible time relationship to the project-specific measures applied and • The event cannot be definitely explained by underlying diseases or other situations.

All SEs are to be documented in the subjects´ file and on the SE report form.

9.3 Reporting of SEs

SEs will be treated according to the Human Research Ordinance (HFV Art. 21). First, the project leader will report any occurring SE to the responsible ethics committee within 7 days. He will also submit a report which evaluates the relationship between the event reported and the methods of collecting health related personal data or sampling of biological material within that project, furthermore proposals how to proceed with the project.

9.4 Reporting of Safety and Protective Measures

The project leader shall notify any immediate safety and protective measures, which have to be taken during the conduct of the research project, the ethics committee within 7 days according to the HFV Art. 20. In addition, the project leader explains the circumstances which necessitated the safety and protective measures.

10 Data - und Quality Management

The principal investigator and the whole study team affirm to uphold the principles of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants will be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals. Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by utilising subject identification code numbers to correspond to treatment data in the computer files. For data verification purposes, authorised representatives of the Sponsor (-Investigator)or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

A good-clinical-practice educated member of the study team is responsible for proper, coded and correct data management. All patient related electronic data is stored coded in a password-protected folder on our institution server. Only dedicated study personel have access. All physical data and patient informed consent is stored in a locked folder at our institution's secretariat. Data storage is only performed in coded form for peer-review. For further informations also see Chapter 8.

11 Statistical Plan

11.1 Determination of Sample Size

Within a study period of 6 to 12 months, all elective and emergency patients scheduled for a Rapid Sequence Induction (RSI) will be included in this study. In 2019, a total of 2'718 general anaesthesias with Rapid Sequence Inductions (RSI) were undertaken at our institution. 275 thereof were children < 18 years of age. Further, 204 Rapid Sequence Inductions were performed in life threatening situations (category: Notfall <1h, vital, sofortiger Eingriff notwendig by the Swiss Society for Anaesthesiology and Resuscitation, A-QUA) where a delay is medically and ethically not acceptable. Further, we estimate that a number of 1000 patients per annum have one or more aspiration risk factors, receiving an advanced laryngeal mask or a regional anaesthesia. In conclusion, we aim to include at least 1500 up to 3200 patients in a one year recruitment period. On basis of the publication of Arzola et al. [36] individual differences in sonography performance can already be detected after 30 to 40 examinations. Although our residents will already have perfomed at least asmany examinations before first patient inclusion, we postulate, that a similar number of patients per capita will be needed to investigate interindividual performance. Given an estimated number of 30 residents and 20 attendings participating, we aim to include 1500 - 2000 patients.

11.2 Statistical Methods

Primary Endpoint:

- Correlation of sonographic estimated gastric volume with volume aspirated through a naso- or orgastric tube.

Secondary Endpoints:

- Performance over time (improvement of examination technique, critical number of examinations).
- Association of performance with experience, residents vs. attendings.
- Number of patients classified as empty -> possible implications for management and induction.
- Number of patients with full stomach -> possible implications for management and induction.
- Time used for examinations, time used with growing experience.
- estimated aspiration risk vs. sonographic gastric volume.
- Total number of pulmonary aspirations.

Collected Variables:

- Patient Demographic: Age, sex, gender, height, weight, BMI, ASA Classification, patient history, concomittant medication, concomitant disease, intervention performed, anaesthetic risk class of the intervention, surgical department of the intervention, urgency of the intervention.
- Sonographer Demographic: education level, years of anaestesiologic experience, years of sonographic experience.
- RSI Indication.
- Last meal/ drink before surgery.
- Subjective estimated aspiration risk (graded by the responsible anaesthetist).
- Sonography quality, reasons for poor quality.

- Sonographic quality of gastric content.
- Sonographic quantity of gastric content.
- Time for examination.
- Effective quantity of gastric content.
- Theoretical change in anaesthesiologic management.
- Reason for not performing gastric sonography.

Analysis:

- Demographic Analysis.
- Institution overall success analysis.
- Interpersonal success analysis with logistic regression an cumulative sum learning curves.
- Analysis of possible changes in anaesthesiologic management.

12 Ethics

12.1 Independent Ethics Committee

Before this project will be conducted, the protocol, the proposed participant information and consent form as well as other project-specific documents will be submitted to a properly constituted Competent Ethics Committee (CEC), for formal approval. The decision of the CEC concerning the conduct of the project will be made in writing to the Sponsor-Project Leader before commencement of this project.

Significant changes to an authorised research project must be approved by the ethics committee before being implemented. Exempt from this requirement are measures which have to be taken immediately in order to protect the participants.

The following are considered to be significant changes:

a. changes affecting the participants' safety and health, or their rights and obligations;

b. a change of research site or conducting the research project at an additional site; or

c. a change of the project leader or sponsor.

The Ethics Committee will be informed within 90 days regarding the termination or completion of the project.

12.2 Ethical Conduct of the Project

This project will be carried out in accordance with principles enunciated in the current version of the Declaration of Helsinki and Swiss regulatory authority's requirements.

12.3 Participant Information and Informed Consent

Prior to the project start each participant has to give their written informed consent after he/she was comprehensively informed - verbally and in writing - on the nature, relevance and impact of the project. The content of this information should be documented on the informed consent. Each participant must be informed that the participation in the project is voluntary and that he/she may withdraw from the project at any time and that withdrawal of consent will not affect his/her subsequent medical treatment. The participants will be given enough time to make their decision whether they would like to participate or not.

The consent to participate into the research project should be signed and dated by both, the participant andthe project leader or a trained study person. A copy of the signed and dated subject information and informed consent form has to be handed out to the participant.

No project related procedures are to be conducted before a legally accepted written informed consent has been given.

13 Confidentiality and Data Protection

Data generation, transmission, archiving and analysis of health related personal data within this project; strictly follow the current Swiss legal requirements for data protection and according to the Ordinance HFV Art. 5. Prerequisite is the voluntary approval of the participant given by signing the informed consent prior start of participation of the research project.

Health related personal data captured during this project from participants are strictly confidential and disclosure to third parties is prohibited; coding will safeguard participants' confidentiality. Confidentiality will be ensured by using coded data. The code will be protected against unauthorized access and will be stored appropriately by the project leader. All patient related date will be destroyed after project termination.

The collected project data may be subject to inspection by the CEC.

14 Funding and Support

No external funding.

15 Compensation

Participants will not be compensated for their participation into this scientific research project.

16 Insurance

Insurance is covered by “Versicherung für klinische Versuche und nichtklinische Versuche“ by Basler Versicherung AG (Policy no.: 30/4.093.845).

Any damage developed during the course of the project is covered by this insurance. So as not to forfeit their insurance cover, the participants themselves must strictly follow the instructions of the project personal. Medical emergency treatment must be reported immediately to the project leader. The project leader must also be informed instantly, in the event of health problems or other damages during or after the course of project.

The project leader will allow delegates of the insurance company to have access to the source data/documents as necessary to clarify a case of damage related to project participation. All involved parties will keep the subjects’ data strictly confidential.

17 Publication Policy

After the statistical analysis of this trial the sponsor and principal investigator will make every endeavor to publish the data in a medical journal.

18 Signatures

The following persons agree with the content of this project by signing this project plan. Changes concerning the responsibilities of every person signing this project plan need to be announced immediately.

Sponsor

This protocol V3.0, 25.01.2021 was subject to critical review and has been approved by the Sponsor-Project Leader. The information herein is consistent with the current risk/benefit assessment and the moral, ethical and scientific principles governing clinical research as set out in the current version of the Declaration of Helsinki.

Prof Dr. med. Michael Ganter

_____ _____

Place, Date Signature

Sponsor - Project Leader

This protocol V3.0, 25.01.2021 was subject to critical review and has been approved by the Sponsor-Project Leader. The information herein is consistent with the current risk/benefit assessment and the moral, ethical and scientific principles governing clinical research as set out in the current version of the Declaration of Helsinki.

Dr. med. Roman Meierhans

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Place, Date Signature

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