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A retrospective analysis of anaesthesia-related morbidity and mortality in horses in a University teaching hospital in the Netherlands.

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Abstract

Objectives: To establish the anaesthesia-related (=AR) mortality and morbidity rate, and the factors influencing them, of all horses undergoing standing sedation (for surgical or diagnostic imaging procedures) or undergoing general anaesthesia in a Dutch equine academic teaching hospital. Furthermore, to determine whether the AR mortality and morbidity rates changed during the past years, compared to previous results from the same hospital and to international published figures.

Study design: A retrospective observational single-centre study.

Research population: In total, 3074 horses anaesthetised or sedated for standing procedures between September 2013 and September 2019.

Methods: All patient information and details of the case were retrieved from patient records. This included presence of potential pre-defined risk factors, as well as occurrence of AR morbidities within 7 days post-anaesthesia and AR mortality status at 7 days post-anaesthesia. For various subsets of the population, AR mortality and morbidity rates were determined. Chi-squared tests and Wald tests were used to establish multivariate logistic regression models to analyse potential risk factors associated with overall AR mortality, overall AR morbidity, AR mild trauma, AR myopathy and AR gastro-intestinal morbidities (e.g. post-anaesthetic colic).

Results: The combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) overall (elective and non-elective cases) AR mortality and morbidity rates were 0.8% and 4.8%, respectively. Restricting the analysis to the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective group solely, percentages decreased to 0.2% and 3.2%, respectively. When the elective group was further restricted to procedures involving general anaesthesia (either surgical cases alone or together with diagnostic cases), the percentages were 0.2% and 3.8%, respectively. For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures, the percentages are 2.5% and 9.6%, respectively.
Multivariate logistic regression models for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective group resulted in significant risk factors for the overall AR morbidity and for two of the three most frequent AR morbidities identified in this study (AR mild trauma and AR gastro-intestinal morbidities). Analysing the AR myopathy in the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures group, did not result in significant associated risk factors, due to the rather small sample size of this analysed group together with the very low incidence of outcome (n=3; 0.13%). The following risk factors showed a significant association with overall AR morbidity: duration of the anaesthesia, season of the year, hypothermia and a turbulent recovery. Furthermore, the following risk factors showed a significant association with AR mild trauma: gender of the patient, anaesthetist training level, hypothermia, a turbulent recovery and the “Other” peri-procedure complications group (combined group of low incidence peri-procedure complications). Hypothermia and a turbulent recovery are risk factors significantly associated with AR gastro-intestinal morbidities (colic, colitis / diarrhoea and typhlitis).
Multivariate logistic regression models for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective group resulted in significant risk factors for the overall AR morbidity and for two of the three most frequent AR morbidities identified in this study (AR mild trauma and AR myopathy). Analysing the AR gastro-intestinal morbidities in the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures group, did not result in significant associated risk factors, due to the rather small sample size of this analysed group together with the very low incidence of outcome (n=4; 0.52%).

The following risk factors showed a significant association with overall AR morbidity: duration of the anaesthesia, season of the year, periods of apnoea (during induction and/or recovery), hypothermia and a turbulent recovery. Furthermore, the following risk factors showed a significant association with AR mild trauma: duration of the anaesthesia, season of the year and a turbulent recovery. Body weight of the patient, body position, duration of the anaesthesia, periods of apnoea (during induction and/or recovery) and problems regarding the intubation are risk factors significantly associated with AR myopathy.

Conclusion: The data suggests a decrease in AR mortality over the past 6 years, compared to both previous data from this clinic and to internationally reported percentages. While AR morbidity may seem to have increased, this is likely due to the different definitions used for some morbidities (especially AR mild trauma) and in this light may actually be lower than the rates previously published by other studies. Further research to refine risk factors (e.g. body condition score instead of body weight) is important so that the AR mortality and morbidity risks can be reduced even further over the coming years. Most importantly, universally accepted definitions of complications and uniform methods to establish outcome need to be drawn up in order for future studies to be less heterogeneous and more directly comparable.

Introduction

Background of the study

The mortality risk associated with anaesthesia in horses is still the highest compared to almost all other domestic animals and humans. Relatively few studies have been conducted to determine this anaesthesia-related (=AR) mortality risk over the past 50 years, with a lot of variation in reported AR mortality risks between the different studies. Studies with the highest level of evidence (according to GRADE classification), concerning prospective multi-centre studies including a large number of cases, found an overall AR mortality risk of 1.6-1.9%, which was reduced to 0.9% when eliminating colic patients from the study population (Johnston, Taylor et al. 1995, Johnston, Eastment et al. 2002, Johnston, Eastment et al. 2004). Prior studies found AR mortality risks in horses varying from 0.63% to 2.2% (Mitchell 1969, Tevik 1983, Young, Taylor 1993, Mee, Cripps et al. 1998a).

More recent studies reported equine AR mortality risk varying from 0.2% to 1.1% (Bidwell, Bramlage et al. 2007, Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015, Dugdale, Obhrai et al. 2016). While the variation among the results of these different studies might be surprising at first, this is mainly due to differences in methods and definitions used to establish AR mortality among the different studies. For example, the study resulting in an AR mortality risk of 0.2%, determined the outcome after 72 hours (Senior, Pinchbeck et al. 2007). While studies with the highest level of evidence, as mentioned before, used 7 days as a time interval for determining the AR mortality risk. The 7-day interval is argued to be long enough, ensuring that more lingering AR mortalities are included, and not to be too long, as this increases the uncertainty of the relation between mortality and the anaesthesia (Johnston 1993). Taking into account the different methods/definitions used among studies and the fact that smaller, single-centre studies are less reliable for overall AR risk estimation (as the influence of site facilities, individual surgeon(s) and anaesthesiologist(s) will be inevitably large), it can be said that there has not been a large decrease in AR mortality risk in horses over the past 50 years. Consequently, the overall AR mortality risk is still approximately 1%, which is in stark contrast with a dramatic risk reduction over the same time frame in humans.

Furthermore, when comparing a horse's overall AR mortality risk with those of humans (0.0047-0.014%)(Arbous, Grobbee et al. 2001, Lienhart, Auroy et al. 2006) or even small animals (0.17%, 0.24%, 1.39%, for dogs, cats, and rabbits, respectively)(Brodbelt, Blissitt et al. 2008) it can be seen that, except for rabbits, there is a big gap between the AR mortality risk of humans and small animals on the one hand and horses on the other. Part of the explanation for the rather large contrast between the reported AR mortality risks of rabbits and horses, as compared to cats and dogs, may be that there is a difference between the risk factors in general, between these different animals. For instance, horses and rabbits are both prey animals, who do not readily show pain/sickness. Therefore, it is harder for an anaesthesiologist to identify pre-existing pain or sickness and intervene adequately at an early stage. Furthermore, horses and rabbits are both herbivores and hindgut fermenters, with a complex and sensitive gastro-intestinal (GI) tract, susceptible to post-anaesthetic colic or ileus (Brodbelt, Blissitt et al. 2008).

The most common causes of AR mortality reported in horses are cardiovascular collapse, fractures, gastro-intestinal causes (post-anaesthetic colic, colitis/diarrhoea, typhlitis), and myopathies. Cardiovascular causes reportedly account for 32-47.6%, fractures for 23-38.1%, gastro-intestinal causes 13-13.1%, and myopathies for 7% of reported equine AR mortalities (Johnston, Eastment et al. 2002, Johnston, Eastment et al. 2004, Bidwell, Bramlage et al. 2007).

As mentioned before, there are relatively few studies detailing AR mortality in horses. However, there are even fewer studies available that focus on equine AR morbidity. The definition of AR morbidity can

differ between the studies. As seen most of the times, AR morbidity is defined as an obtained illness or injury caused by the anaesthesia, which you can usually assign specifically to one or more peri-procedural complications (e.g. hypotension during the anaesthesia). Another definition used in research is the collection of all non-fatal illnesses or injuries due to the anaesthesia.
The AR morbidity risk in available studies varies from 1.4% to 15.8% (Young, Taylor 1993, Johnston, Eastment et al. 2004, Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015). Studies with smaller numbers of cases show a more severe AR morbidity risk. Therefore, their reliability may be questionable. Nevertheless, the difference in reported AR morbidity risk in horses is still quite large. Arguably the most reliable study to date, being a prospective multi-centre study including n = 8242 horses, found an AR morbidity risk of approximately 2.7% (Johnston, Eastment et al. 2004). However, this percentage only includes non-fatal morbidities, which could lead to a slightly smaller AR morbidity risk. The most common AR morbidities reported were post-anaesthetic colic and post-anaesthetic lameness (for which myopathy was the most important cause). The reported incidences of these individual morbidities vary even more between the different studies than the overall AR morbidity risk. Post-anaesthetic colic accounts for 45-63.8% and post-anaesthetic lameness for 5-73.7% of all AR morbidities, depending on the study (Richey, Holland et al. 1990, Young, Taylor 1993, Johnston, Eastment et al. 2004, Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015).

These differences in the AR morbidity risk and the differences in the relative incidence of the different morbidities is mostly caused by the lack of consistency between studies due to the absence of universally agreed definitions used to identify the different morbidities. Moreover, most of these results are based on small, single-centre retrospective studies. Therefore, these studies contain low levels of external validity. In addition, the population of horses differs markedly between countries. For example, the proportion of thoroughbreds versus large, heavy warmblood horses varies significantly between the UK and the Netherlands. Therefore, the results of a UK-based study might not be equally applicable to the population of horses in the Netherlands. The same goes for older studies (>10-20 years ago), in which halothane was commonly used instead of isoflurane, which is mostly used nowadays. Also, invasive blood pressure measurement and management was not very common > 20 years ago compared to the present.

Risk factors for AR mortality and morbidity

Over the last 50 years, several studies have described risk factors associated with AR mortality in horses. Most risk factors were first identified using univariable logistic regressions. These studies suggest that the following factors could influence the AR mortality risk: age, pregnancy (third trimester), season of the year, procedure type, premedication, induction agents, maintenance agent, body position, duration of anaesthesia/procedure, and start time of anaesthesia/procedure (Johnston, Taylor et al. 1995, Mee, Cripps et al. 1998). Later, several multivariate logistic regressions found the following factors to have a significant effect on equine AR mortality risk: age, ASA classification, procedure type, method of anaesthetic induction in combination with maintenance, day of the week (workday or weekend), and start time of anaesthesia/procedure (Johnston, Eastment et al. 2002, Johnston, Eastment et al. 2004). A more recent study also added the ASA-classification to the list of significant underlying factors for AR mortality risk (Dugdale, Obhrai et al. 2016).

As noted, few studies investigated risk factors for specific AR morbidities in horses. Using univariable logistic regressions, it was shown that increased duration of anaesthesia and hypotension during surgery carry an increased risk of developing post-anaesthetic lameness due to myopathy or neuropathy (Richey, Holland et al. 1990). Furthermore, using multivariate logistic regression, another study found that the duration of anaesthesia and body position were identified as risk factors for post-anaesthetic lameness (Johnston, Eastment et al. 2004). Moreover, a smaller study found increased body weight to be a significant risk factor for post-anaesthetic lameness, however this was only the case for non-surgical procedures (Franci, Leece et al. 2006). A more recent study, using univariable

logistic regressions, found that age, weight, breed, usage of the horse, and perioperative antimicrobial administration were significant risk factors for development of post-anaesthetic colic (Jago, Corletto et al. 2015). The same authors performed a multivariate regression, suggesting that breed, perioperative administration of sodium benzylpenicillin, and perioperative administration of butorphanol were significant factors regarding the risk for post-anaesthetic colic. A study looking into fasting as a risk factor for post-anaesthetic colic found an incidence of 2.5% (Bailey, Hague et al. 2016) which seems considerably lower than the incidence rate of 10.5% reported elsewhere (Jago, Corletto et al. 2015). This would suggest that pre-operative fasting could be a risk factor for developing post-anaesthetic colic.

Aside from risk factors for the specific morbidities mentioned above, there are no studies investigating risk factors for other anaesthesia-related morbidities (e.g. AR mild trauma). Moreover, there are no studies that examine potential risk factors associated with the overall AR morbidity (the development of one or more AR morbidities) risk in horses.

Development in anaesthetics

The most recent data used to investigate the AR mortality and morbidity risks dates back to anaesthetic procedures performed in 2013 (Dugdale, Obhrai et al. 2016) and the last larger multi-centre study even dates back to anaesthetic procedures performed in 1999 (Johnston, Eastment et al. 2004). However, over the last 21 years, there has been a continuous development in anaesthetic management. Consequently, it is questionable whether the AR mortality and morbidity risks are still the same. Furthermore, the same question holds for the relative incidence of the identified risk factors.

Besides the fact that most of the available information may be outdated, there is also a lot of information that still needs to be collected. Determination of risk factors regarding AR morbidity is still incomplete. Also, there may be other possible factors that might significantly affect AR mortality or morbidity, which have not yet been examined, such as body condition score (=BCS). Although body weight has been examined extensively in prior research, no study has investigated whether being underweight or overweight has a significant effect on equine AR mortality or morbidity.

It is important to keep our knowledge about equine AR mortality and morbidity risks up-to-date, as this plays an important role in the consideration whether or not to perform surgery or diagnostic procedures under general anaesthesia or during standing sedation, or even whether to proceed with the procedure at all, for owners as well as veterinarians. Moreover, expanding our knowledge and understanding of the underlying risk factors will contribute to decreasing the AR mortality and morbidity risks, because this information can lead to further optimization of anaesthetic management.

Aim of the study

The aim of this study is to establish the AR mortality and morbidity risk in horses undergoing general anaesthesia over a period of six years (2013-2019) in a Dutch equine academic teaching hospital. Furthermore, this study aims to identify the relative incidence of each of the causes of AR mortality and the different types of AR morbidities. The overall research question for this study is: How high is *the anaesthesia-related mortality and morbidity risk in this hospital, and which underlying factors influence them and to what extent?* By answering the question above we can also answer another question, namely: *Has the AR mortality and morbidity risk decreased in the past years*, *compared to previous analyses in our own clinic, and how do these risks compare to internationally reported percentages?* These questions result in the following hypotheses:

- *The AR mortality risk for elective cases under general anaesthesia decreased in the past years.*
- *The AR mortality risk for elective cases under general anaesthesia is lower compared to internationally reported percentages.*

- *The AR morbidity risk for elective cases under general anaesthesia decreased in the past years.*
- *The AR morbidity risk for elective cases under general anaesthesia is lower compared to internationally reported percentages.*

In the following figure, a conceptual framework is given with all the potential factors (variables) and their expected relation (arrows) to AR mortality and/or morbidity. This framework is used as the basis for this study.

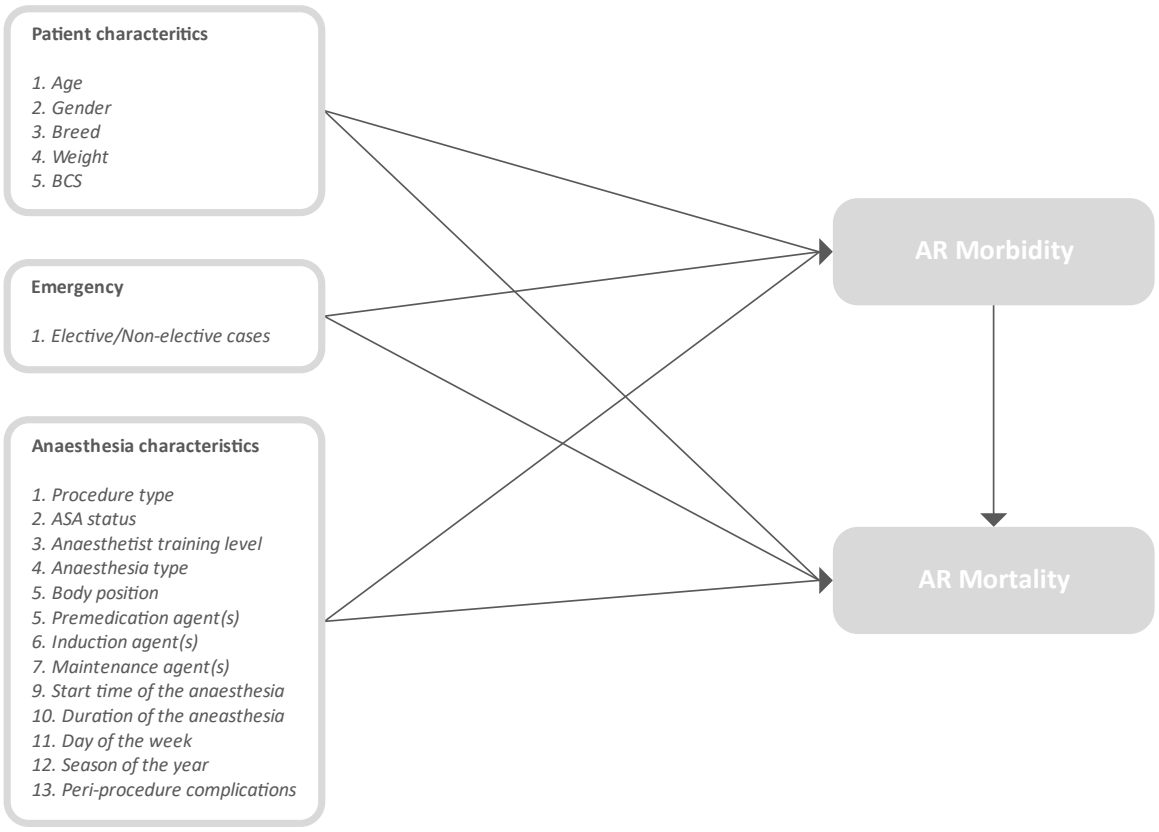

Figure 1: Conceptual framework.

Materials and Methods

Data collection

Data of all patients undergoing standing sedation for surgical or diagnostic imaging procedures or undergoing general anaesthesia at the Department of Equine Sciences at Utrecht University, from 1 September 2013 until 1 September 2019 were collected prospectively. In total, information about 3074 clinical cases were gathered at the time of anaesthesia. Anaesthesia records of every anaesthetic event were entered into the electronic patient files in a patient information management software system (AGFA Healthcare - Vetware, Version 0430.0160). The occurrence of peri-operative complications, morbidities or mortality were recorded in a separate logbook. Most of the complications to be recorded by the anaesthetist were predefined and given as a list of options, as shown in table 2.

		Definition	Duration
Tachypnoea	*Adult horse*	**RR >30**	>30 minutes
	Foal	**RR >50**	>30 minutes
	Donkey	**RR >40**	>30 minutes
Bradycardia	*Adult horse*	**HR <20**	>30 minutes
	Foal	**HR <60**	>30 minutes
	Donkey	**HR <25**	>30 minutes
Tachycardia	*Adult horse*	**HR >50**	>30 minutes
	Foal	**HR >120**	>30 minutes
	Donkey	**HR >60**	>30 minutes
Hypotension		**MAP <50 mmHg**	>30 minutes
Hypertension		**MAP >100 mmHg**	>30 minutes
Hypothermia		**T <36 °C**	>30 minutes
Acidosis	*Metabolic*	**<7.25 pH**	>30 minutes
	Respiratory	**<7.25 pH**	>30 minutes
Alkalosis	*Metabolic*	**>7.55 pH**	>30 minutes
	Respiratory	**>7.55 pH**	>30 minutes
Hypoxemia		**PaO_2 < 50 mmHg**	>30 minutes
Hypercapnia		**PaO_2 > 80 mmHg**	>30 minutes

Table 2: Predefined definitions of peri-procedural complications.

Every entry in the notebook was entered in an electronic table (*Microsoft Excel, 2016*) whereafter the data was checked against the corresponding electronic case records for un-/misreported data and complemented with any missing variables (e.g. age). For each case, the following data were collected: Age, gender, weight, BCS, breed, ASA status, day of the week, season of the year, start time of anaesthesia, duration of anaesthesia, anaesthetist training level, procedure type, anaesthesia type, premedication agent(s), induction agent(s), maintenance agent(s), body position, occurrence of

(predefined) peri-procedural complications, post-anaesthetic AR morbidities (within 7 days post-anaesthesia), mortality status (at 7 days post-anaesthesia) and where applicable cause of death.

Peri-procedural complications are defined as all complications occurred soon before, during or soon after the anaesthesia (e.g. hypothermia during the anaesthesia), which could lead to an illness or injury.
AR morbidity is defined as an obtained illness or injury caused by the anaesthesia, which you can usually assign specifically to one or more peri-procedural complications (e.g. hypotension during the anaesthesia).
Mortality status could be one of the following outcomes: alive, AR death or non-AR death. A patient was considered as an "AR death" if the horse died because of AR-complications/AR-morbidities, or when the horse was euthanized because of AR-complications/AR-morbidities which were incompatible with life.

Age was recorded as a continuous variable in days. Before analysis, patients were divided into 7 age groups as shown in figure 3. Gender was recorded as stallion, gelding or mare. Breeds were stratified to cold blood/draft horse, warm blood and thoroughbred. The weight of the patient was analysed as a continuous variable in kilograms. The BCS was a number from 1 to 5, where 1 stands for severely underweight and 5 for severely overweight (Kuiper, van Nieuwstadt 2016).

All surgical procedures were classified into 6 main categories, with some categories having subgroups, giving a total number of 14 classes. An overview of these procedures is given in figure 7. In all cases an anaesthetist conducted a physical examination before the anaesthesia started. Based on these findings the patient was assigned an ASA physical status score, according to the standards set by the *American Society of Anesthesiologists*. The ASA physical status classification is an integer varying from 1 to 5, where 1 stands for a normal healthy patient and 5 for a moribund patient who is not expected to survive without surgery. All anaesthetists were grouped according to their level of anaesthesia training, namely: intern, resident, or specialist (ECVAA diplomate). When more than one anaesthetist was involved in the procedure, the highest ranked anaesthetist was considered as responsible and therefore that level was recorded.

The anaesthetic procedures were classified into 4 main categories, namely: standing sedation, general anaesthesia – inhalation, general anaesthesia – TIVA, and combination anaesthesia. Anaesthesia where a combination of anaesthetic procedures (standing sedation, general anaesthesia – inhalation or general anaesthesia – TIVA) were performed consecutively (i.e., an anaesthetic procedure where prolonged standing sedation was followed by general anaesthesia, or where TIVA was followed by inhalation anaesthesia) were recorded as combination anaesthesia. Furthermore, the general anaesthesia – inhalation and the combination anaesthesia classes both had subgroups specifying the mode of ventilation, namely: spontaneous breathing, IPPV, and IPPV + PEEP. This results in a total of 8 categories. The subgroup within 'combination anaesthesia' was determined by the mode of ventilation during general anaesthesia. When anaesthesia included a combination of spontaneous and mechanical ventilation, only one was recorded in the following order of preference: IPPV + PEEP, IPPV, or only spontaneous breathing. Figure 10 shows the different anaesthetic procedures considered.

All procedures were performed with the patient in a specified body position. If during one procedure a combination of positions was used, the position in which the patient was maintained the longest was recorded as overall body position. A total of 6 groups of possible premedication agents were distinguished. These either consisted of a single agent or a combination of multiple agents. For the induction agents, 6 groups were defined, including "none", which was applicable for standing sedations, as shown in figure 13.

All agents used for maintenance were recorded, resulting in a total of 24 different combinations (PIVA) of maintenance agents. Among these combinations there were many with very low frequencies of use. Therefore, all combinations with a frequency of 2% or lower were combined in one group, namely: 'Other'. Figure 14 shows the remaining maintenance agent categories.

The start time of anaesthesia was categorized into four groups, with an equal interval of 6 hours starting at 12 'o clock midnight. The duration of anaesthesia was measured in hours and analysed as a continuous variable. The day of the week was categorized into 2 groups, namely: weekday and weekend. Seasonal influence on outcome was measured by categorizing all procedures into 4 groups determined by time of the year in quarters.

All noted peri-procedural complications were merged into larger groups, based on their clinical similarities and relevance. Since one patient can have multiple complications in one procedure, every category of complication was a binary variable on its own. A total of 18 different complication classes were established.

All noted AR morbidities were merged into larger groups, based on similar aetiology and clinical relevance. Since one patient can have multiple AR morbidities in one procedure, every AR morbidity group was a binary variable on its own. A total of 6 different morbidity groups were established, namely: "Musculoskeletal - Myopathy, neuropathy, laminitis, other", "Musculoskeletal - Muscle / tendon tear and fractures", "Gastro-intestinal" (colic, colitis / diarrhoea and typhlitis), "Respiratory related" (e.g. aspiration pneumonia), "Trauma - mild" (wounds, bruises, hematomas and ocular trauma including corneal erosions) and "Other".

Statistical analysis

At first, the all-cause overall AR mortality and morbidity risk was determined, together with their corresponding incidence of causes of death and morbidity type, respectively. Thereafter, the population was divided into elective and non-elective case groups. All procedures that were classified as emergencies were placed in the non-elective procedures group. All other cases were placed in the elective procedures group. The same risks and incidences as described above were determined for each individual group. For the benefit of cross-study comparison, the overall and elective procedures group is divided into four categories, namely: general anaesthesia (with two sub groups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic), for which the AR mortality and morbidity risk is also determined.

The collected patient data were investigated as potential underlying risk factors using univariate analysis with chi-squared tests for categorical variables and the Wald test for continuous variables to test their influence on outcome (i.e. AR mortality status at day 7). All analysed variables with a likely association with the outcome ($p < 0.4$) were included in the build-up for a multivariate logistic regression model. The multivariate logistic regression was built using a backward build-up method, where all previously selected variables are removed if they do not significantly improve the fit of the model (LR test -χ^2- $p > 0.05$), resulting in a *preliminary main effects model*. Thereafter, all continuous independent variables were tested for linearity to the log odds of the dependent variable, via the Box-Tidwell procedure using a Bonferroni corrected *p*-value (Tabachnick, Fidell 2014). This results in the *main effects model*. Where present, clinically relevant pairs of variables in the main effects model were tested for interaction with each other. All significant interaction terms (Wald statistic $p < 0.05$ or LR test -χ^2- $p < 0.05$) were added to the main effects model, resulting in the *preliminary logistic regression model*. The fit of the model was assessed using the Pearson (i.e. Hosmer-Lemeshow) goodness-of-fit test. Odds ratios are given in the *final logistic regression model* along with their corresponding *p*-values

and their confidence intervals (CI 95%). All statistical analyses were performed using *IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.*

The same statistical steps as described above, were repeated for overall AR morbidity (the development of one or more AR morbidities) as well as for the three most frequent AR morbidity classes identified in the two different groups (elective and non-elective group) in the study population.

Results

Data description

Patient characteristics

Age

The study population consisted of a total of 3074 different cases pertaining to 2592 individual patients. Patient age ranged from 1 day to 36 years, with a mean of 9 years and 10 months and a standard deviation of 6 years and 5 months. In 24 cases the age is missing. The distribution of the age is shown in figure 3.

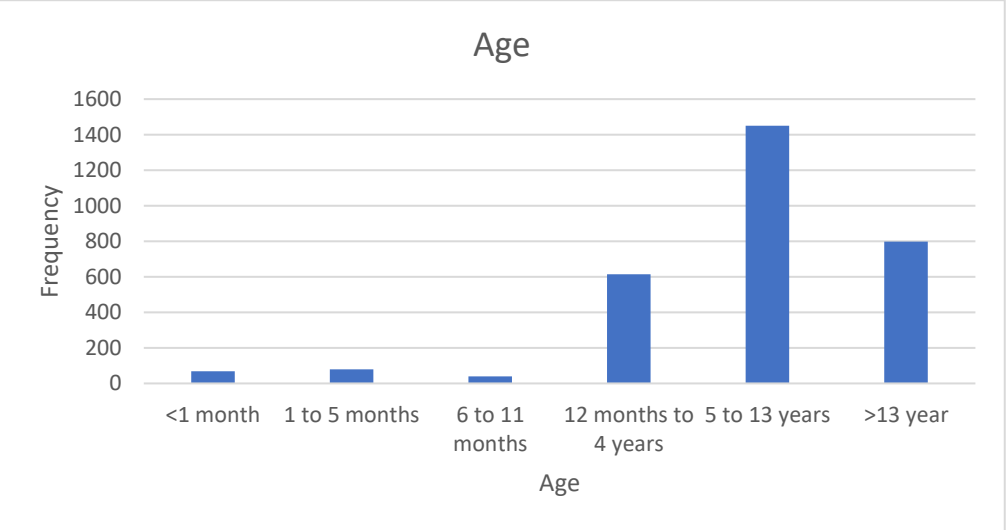

Figure 3: Age distribution (n=3050).

Gender and breed

The distribution of gender and breed is shown in table 4.

		Breed			Total
		Cold blood	*Warm blood*	*Thoroughbred*	
Gender	*Stallion*	120	322	21	**463**
	Gelding	371	798	25	**1194**
	Mare	396	985	36	**1417**
Total		**887**	**2105**	**82**	**3074**

Table 4: Gender/Breed frequencies.

Weight

The weight of horses in the study population ranged from 13 to 903 kg, with a mean of 478 kg and a standard deviation of 163 kg. In 259 (of the 3074) cases the body weight was missing. The distribution of body weight is shown in figure 5.

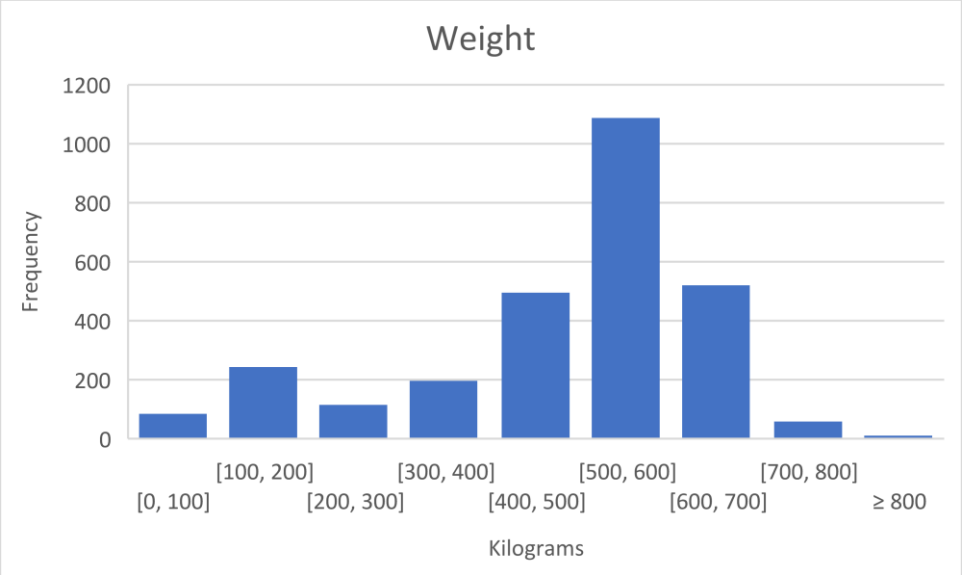

Figure 5: Weight distribution (n=2815).

BCS

Unfortunately, the majority of the cases were not provided with a BCS in the pre-anaesthetic exam record. Specifically, there were only 1156 cases with a valid BCS (i.e., 1918 cases missing). Figure 6 shows the distribution of BCS in the current study sample.

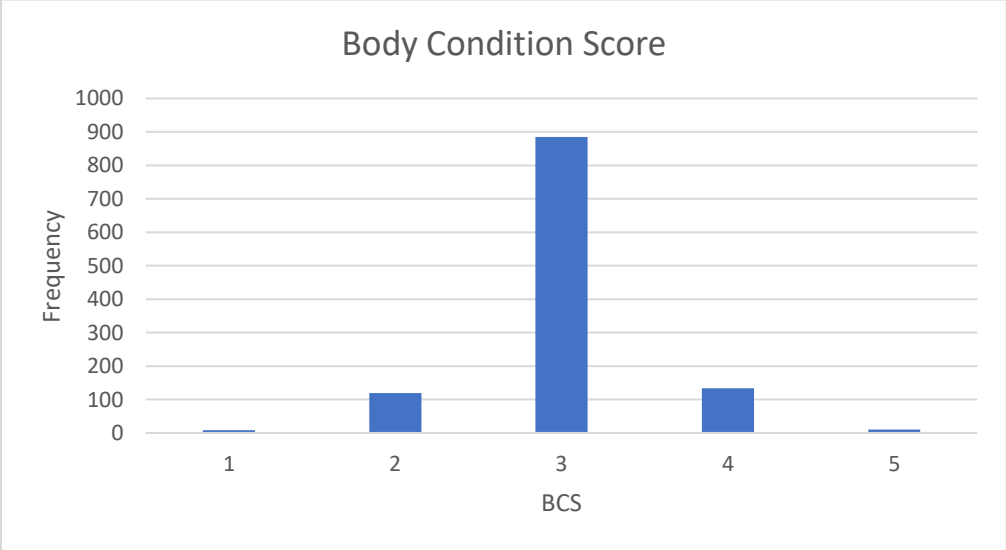

Figure 6: BCS distribution (n=1156).

Emergency

Elective/ Non-elective cases

Of the 3074 cases, 2305 cases were elective procedures and 769 cases were non-elective procedures. The distribution of various procedure types within both the elective and non-elective group is shown in table 21.

Anaesthesia characteristics

Procedure type

An overview of the different procedures, with their corresponding frequencies, are given in figure 7.

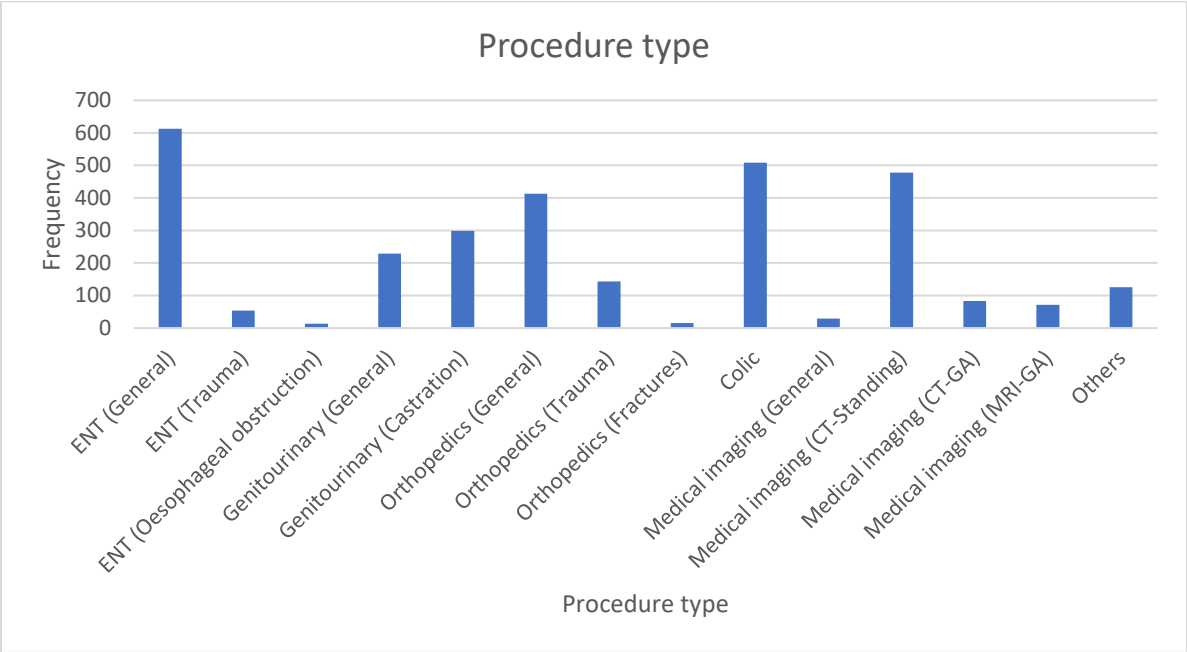

Figure 7: Procedure type frequencies (n=3074).

ASA

Figure 8 shows the frequency distribution of ASA classification among the different cases.

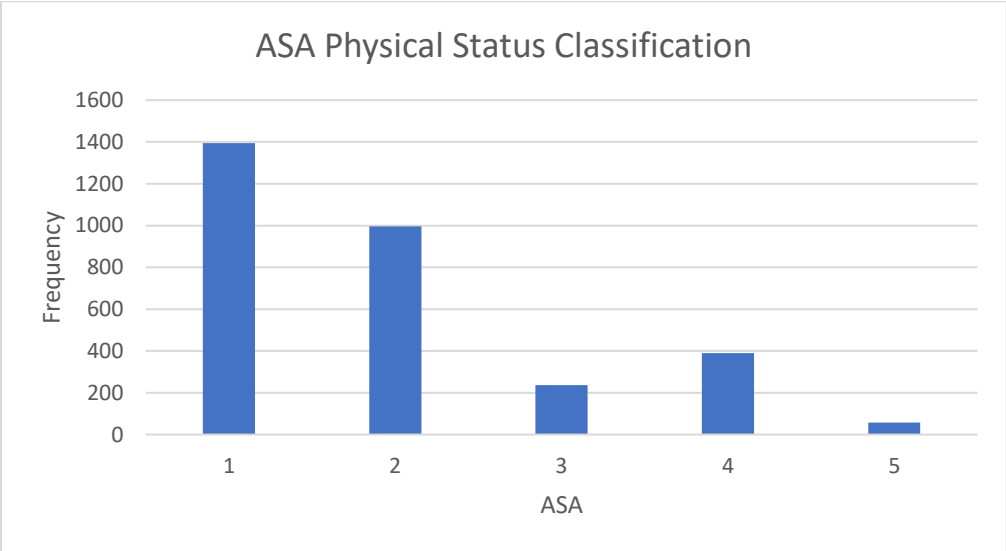

Figure 8: ASA Physical Status Classification frequencies (n=3074).

Anaesthetist training level

Figure 9 shows the frequency distribution of anaesthetic events by anaesthetist training level.

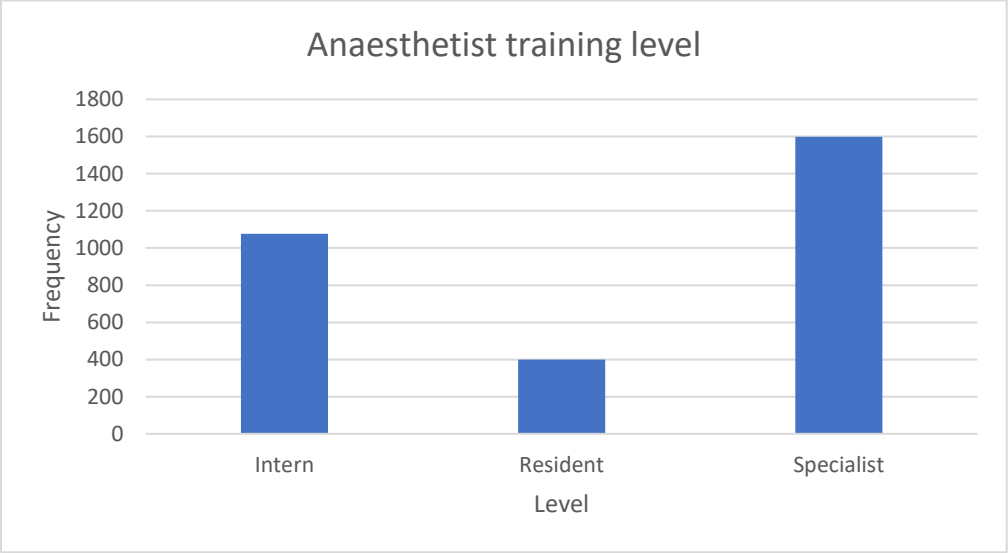

Figure 9: Anaesthetist training level frequencies (n=3074).

Anaesthesia type

In 16 (of the 3074) case records the anaesthesia type was missing. Figure 10 shows the frequencies of the different anaesthesia types.

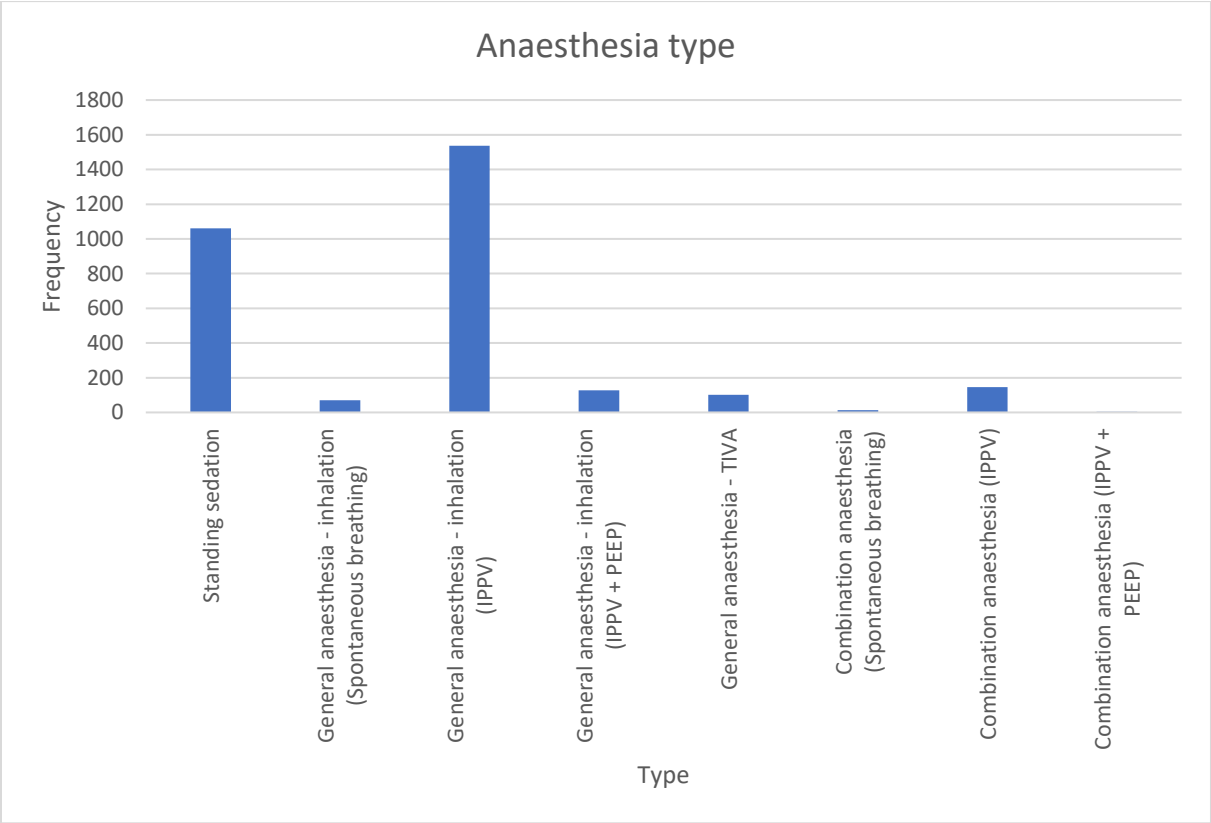

Figure 10: Anaesthesia type frequencies (n=3058).

Body position

Figure 11 shows the frequencies of the different body positions.

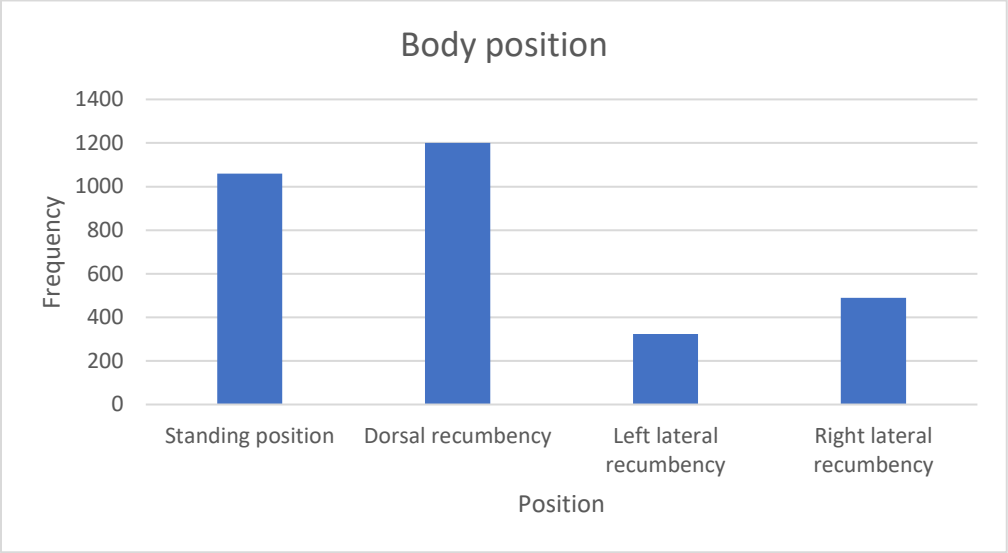

Figure 11: Body position frequencies (n=3074).

Premedication agent(s)

In 14 (of the 3074) cases the premedication agents were missing. Figure 12 shows all the different premedication agent(s) groups, together with their frequencies.

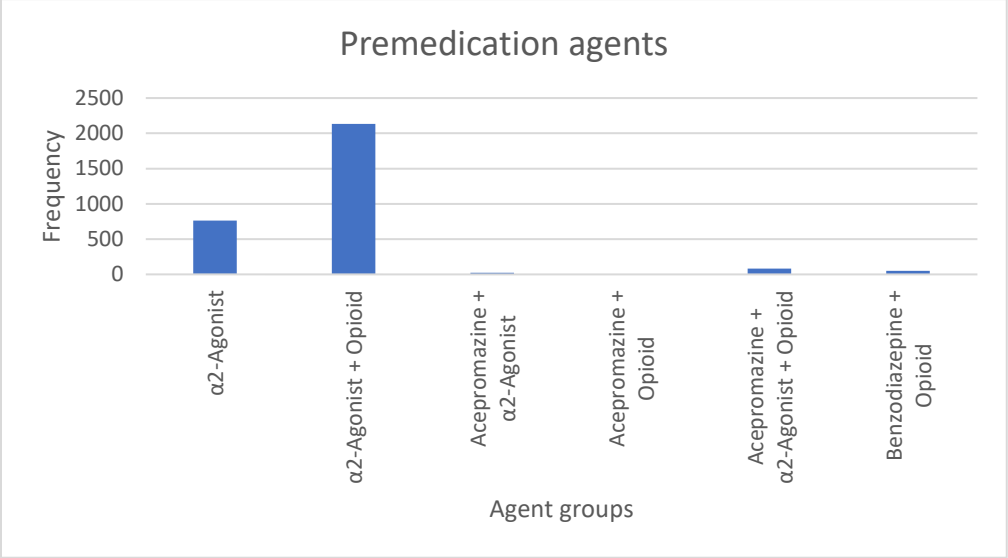

Figure 12: Premedication agent(s) frequencies (n=3060).

Induction agent(s)

In 9 (of the 3074) cases the induction agents were not recorded. Figure 13 shows all the different induction agent(s) groups, together with their frequencies.

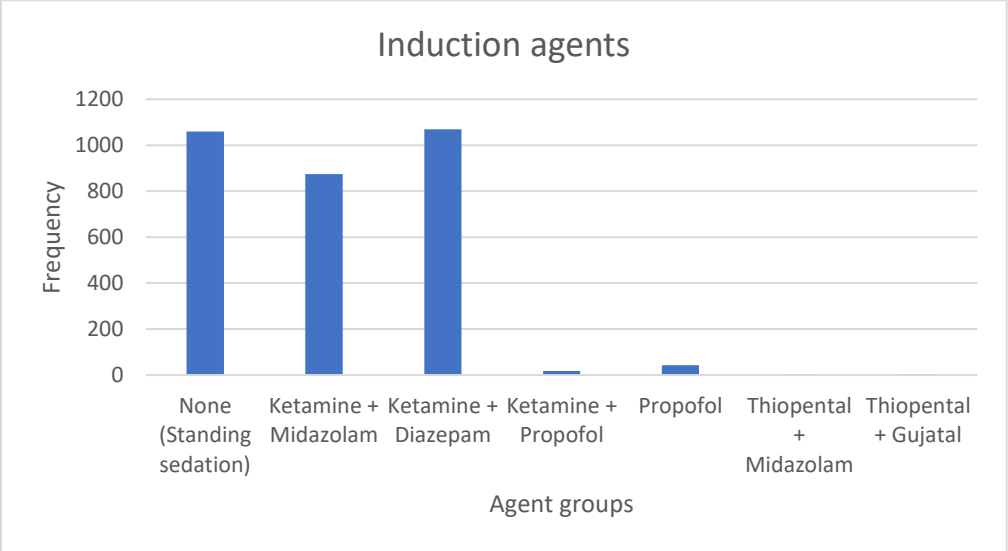

Figure 13: Induction agent(s) frequencies (n=3065).

Maintenance agent(s)

In 15 (of the 3074) cases the maintenance agents were missing. Figure 14 shows all the different maintenance agent(s) groups, together with their frequencies.

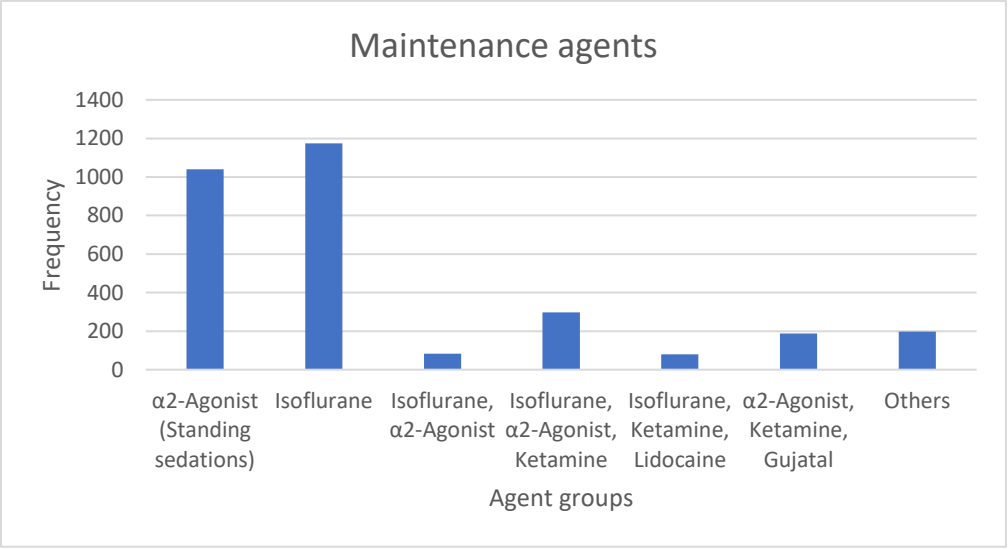

Figure 14: Maintenance agent(s) frequencies (n=3059).

Start time of the anaesthesia

In 645 (of the 3074) case records the start time of the anaesthesia was missing. The frequencies of each group is shown in figure 15.

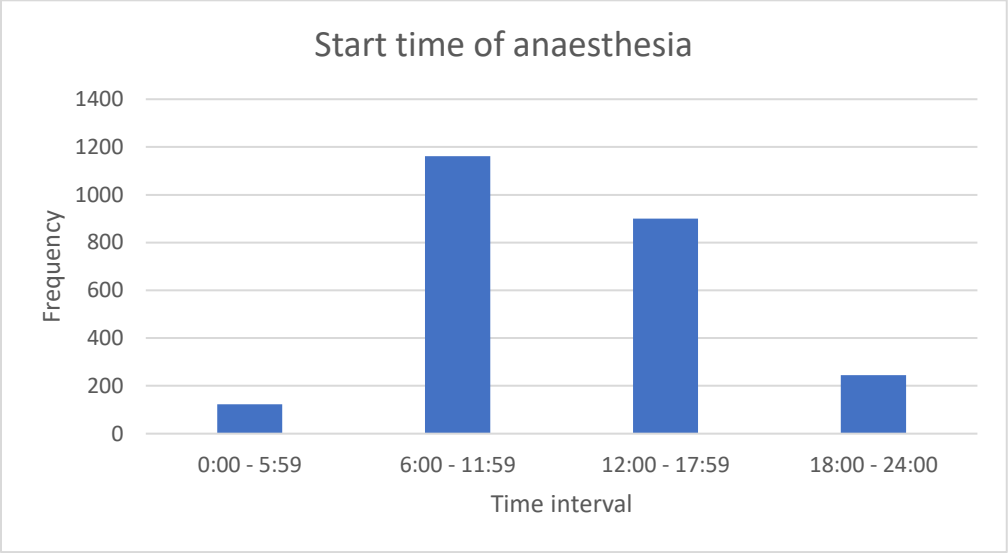

Figure 15: Anaesthesia starting time frequencies (n=2429).

Duration of anaesthesia

The duration of anaesthesia ranges from 5 minutes to 7 hours and 34 minutes, with a mean duration of 1 hour and 55 minutes, a median of 1 hour and 40 minutes and a standard deviation of 62 minutes. There were 2384 valid entries, thus 692 duration entries were missing. The frequency distribution of the duration of anaesthesia (in hours) is shown in figure 15.

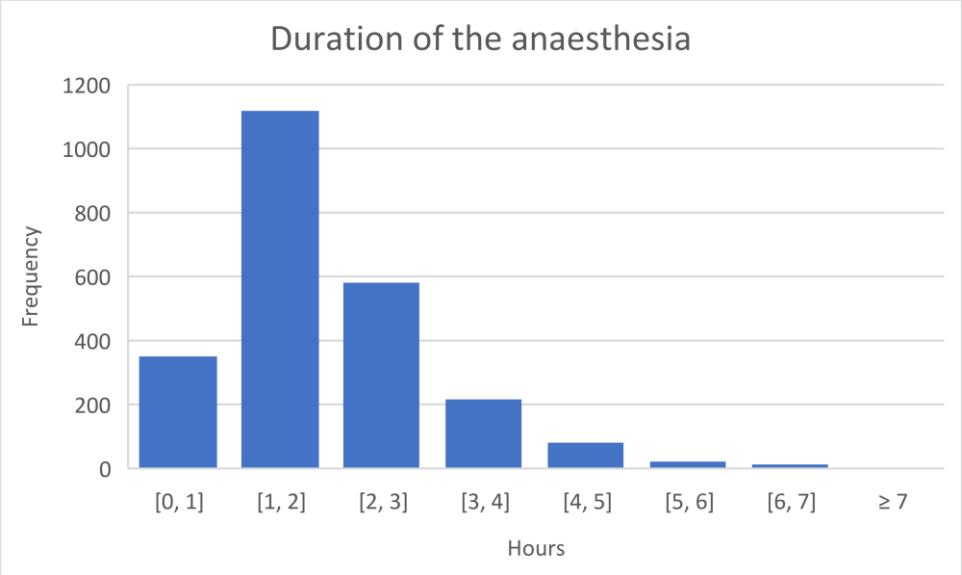

Figure 16: The distribution of the anaesthesia duration (n=2384).

Day of the week

The frequencies of the two groups (weekday and weekend) are shown in figure 17.

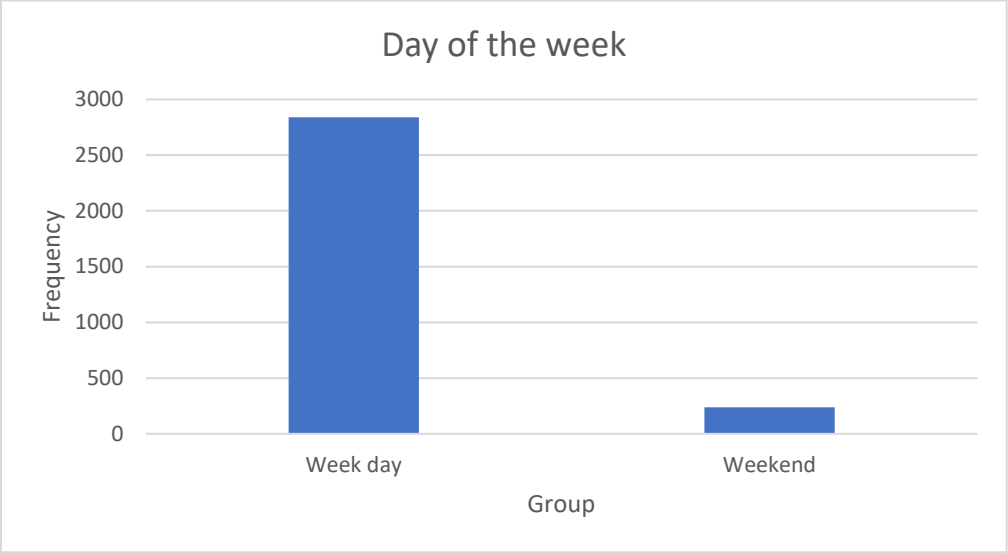

Figure 17: Day of the week frequencies (n=3074).

Season of the year

Frequencies of the different seasons are shown in figure 18.

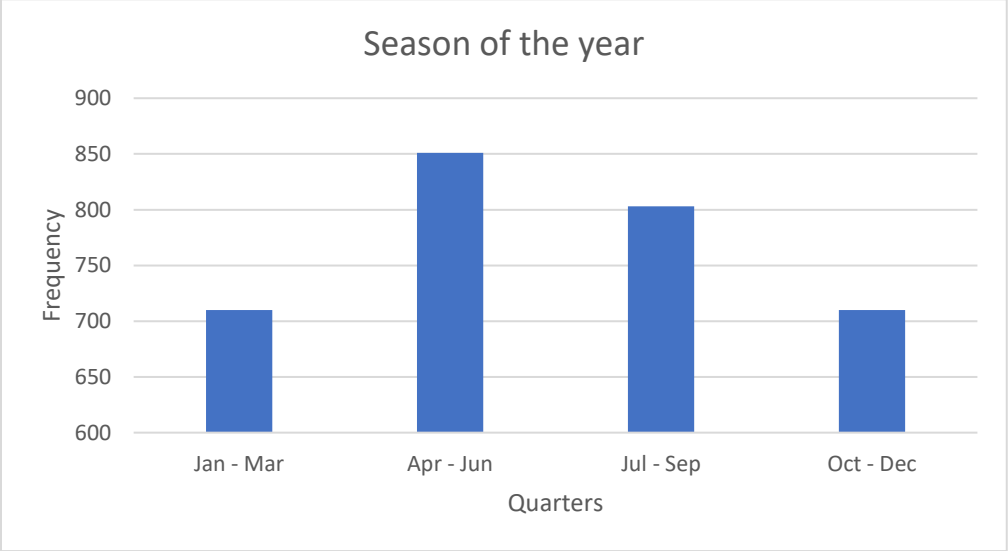

Figure 18: Season of the year (quarters) frequencies (n=3074).

Peri-procedural complications

Table 19 shows the incidence of the different peri-procedural complications and the overall incidence of procedures with one or more complications.

		Occurred		Total
		Yes	*No*	
Complication	*Respiratory – Tachypnoea*	11	3063	**3074**
	Respiratory – Dyspnoea	76	2998	**3074**
	Respiratory – Apnoea	12	3062	**3074**

	Circulatory - Brady / Tachycardia	57	3017	**3074**
	Circulatory - Hypotension	23	3051	**3074**
	Circulatory - Hypothermia	77	2997	**3074**
	Circulatory - Acidosis	57	3017	**3074**
	Circulatory - O2 / CO2 Imbalance	40	3034	**3074**
	Circulatory - Electrolyte imbalance	340	2734	**3074**
	Circulatory - Pathological arrhythmia	17	3057	**3074**
	Circulatory - Other	263	2811	**3074**
	Problems intubation	18	3056	**3074**
	Problems extubation	8	3066	**3074**
	Turbulent recovery	213	2861	**3074**
	Insufficient depth of anaesthesia	369	2705	**3074**
	Bleeding - from trauma	33	3041	**3074**
	Bleeding - without trauma	4	3070	**3074**
	Other	66	3008	**3074**
Complications	*Overall incidence*	**1095** (35.6%)	**1979**	**3074**

Table 19: Complication frequencies and the overall incidence of procedures with one or more complications.

AR morbidity

Morbidities

Table 20 shows the incidence of the different AR morbidity groups and the overall incidence of procedures with one or more AR morbidities.

		Occurred		Total
		Yes	*No*	
AR Morbidity	*Musculoskeletal - Myopathy, neuropathy, laminitis, etc.*	34	3042	**3074**
	Musculoskeletal - Muscle / tendon tear and fractures	3	3073	**3074**
	Gastro-intestinal	21	3055	**3074**
	Respiratory	4	3072	**3074**
	Trauma – Mild	83	2993	**3074**
	Other	16	3060	**3074**
AR Morbidities	*Overall incidence*	**148** (4.8%)	**2926**	**3074**

Table 20: AR morbidity groups frequencies and the overall incidence of procedures with one or more AR morbidities.

All-cause AR mortality and morbidity risks and incidences

AR mortality and morbidity risk

Of the total of 3074 cases, 24 patients were considered as an "AR death" (died/euthanized because of occurred AR-complications/AR-morbidities), 273 patients died or were euthanized due to reasons not associated with anaesthesia (e.g. infaust prognosis of surgery, fatal surgical complications, etc.), and 2777 patients were alive at 7 days post the procedure. This results in an all-cause AR mortality risk of 0.8%. Most of these AR mortalities were found in the non-elective group, especially during colic procedures (n=17). When we separate the research population into elective and non-elective procedures, we get an all-cause AR mortality risk of 0.2% and 2.5%, respectively.
Of the total of 3074 cases, 148 patients developed one or more AR morbidities. This results in an all-cause AR morbidity risk of 4.8%. Again, most of these AR morbidities were found in the non-elective group, especially during colic procedures (n=59). When we separate the research population into elective and non-elective procedures, we get an all-cause AR morbidity risk of 3.2% and 9.6%, respectively.

			Mortality status			Total	Morbidity	
			AR dead	*Alive*	*Non-AR dead*		*Yes*	*No*
Procedure	Elective	*ENT (General)*	2	599	3	**604**	29	575
		ENT (Trauma)	0	35	0	**35**	1	34
		ENT (Oesophageal obstruction)	0	1	1	**2**	0	2
		Genitourinary (General)	1	172	1	**174**	9	165
		Genitourinary (Castration)	1	295	0	**296**	7	289
		Orthopedics (General)	1	387	9	**397**	10	387
		Orthopedics (Trauma)	0	22	3	**25**	1	24
		Orthopedics (Fractures)	0	8	0	**8**	1	7
		Medical imaging (General)	0	21	5	**26**	0	26
		Medical imaging (CT-Standing)	0	463	12	**475**	8	467
		Medical imaging (CT-GA)	0	69	9	**78**	2	76
		Medical imaging (MRI-GA)	0	66	5	**71**	4	67
		Others	0	94	20	**114**	2	112
	Total		*5* (0.2%)	*2232*	*68*	*2305*	*74* (3.2%)	*2231*
	Non-Elective	*Colic*	17	314	177	**508**	59	449
		ENT (General)	0	9	0	**9**	0	9
		ENT (Trauma)	0	19	0	**19**	0	19

	ENT (Oesophageal obstruction)	1	8	2	**11**	1	10
	Genitourinary (General)	1	46	8	**55**	4	51
	Genitourinary (Castration)	0	3	0	**3**	1	2
	Orthopedics (General)	0	13	3	**16**	2	14
	Orthopedics (Trauma)	0	111	7	**118**	6	112
	Orthopedics (Fractures)	0	7	0	**7**	0	7
	Medical imaging (General)	0	0	3	**3**	0	3
	Medical imaging (CT-Standing)	0	3	0	**3**	0	3
	Medical imaging (CT-GA)	0	2	3	**5**	0	5
	Others	0	10	2	**12**	1	11
	Total	*19 (2.5%)*	*545*	*205*	*769*	*74 (9.6%)*	*695*
Total		**24 (0.8%)**	**2777**	**273**	**3074**	**148 (4.8%)**	**2926**

Table 21: Mortalities and morbidities (at 7 days post procedure).

For the benefit of cross-study comparison, the overall and the elective group is divided even further into four categories, namely: general anaesthesia – surgical, general anaesthesia – diagnostic, standing sedation – surgical and standing sedation – diagnostic. The incidence of AR mortality and morbidity, along with their corresponding percentages, in these individual groups can be seen for the overall group in table 22 and for the elective group in table 23.

			AR Mortalities		Total	AR Morbidities	
			n	*%*		*n*	*%*
Procedure	General anaesthesia	*Surgical*	21	**1.1**	1846	115	**6.2**
		Diagnostic	0	**0.0**	168	6	**3.6**
		Total	21	**1.0**	2014	121	**6.0**
	Standing sedation	*Surgical*	3	**0.5**	567	19	**3.4**
		Diagnostic	0	**0.0**	493	8	**1.6**
		Total	3	**0.3**	1060	27	**2.5**
Total			24	**0.8**	3074	148	**4.8**

Table 22: Overall AR Mortalities and morbidities (at 7 days post procedure).

			AR Mortalities		Total	AR Morbidities	
			n	*%*		*n*	*%*
Procedure	General anaesthesia	*Surgical*	2	**0.2**	1133	43	**3.8**
		Diagnostic	0	**0.0**	160	6	**3.8**
		Total	2	**0.2**	1293	49	**3.8**

	Standing sedation	*Surgical*	3	**0.6**	522	17	**3.3**
		Diagnostic	0	**0.0**	490	8	**1.6**
		Total	3	**0.3**	1012	25	**2.5**
Total			5	**0.2**	2305	74	**3.2**

Table 23: AR Mortalities and morbidities in the elective group (at 7 days post procedure).

Causes and timing of AR death

All causes of AR mortalities are noted, together with the phase of anaesthesia during which mortality occurred. The anaesthesia phases included premedication, induction, maintenance, recovery, and aftercare. Table 24 shows all causes of AR deaths along with their corresponding percentage incidence and AR mortalities frequencies (and percent's) per part of the anaesthesia. As table 24 shows, most AR mortalities were due to pathological arrhythmias/cardiac arrests (n=8; 33.3%) followed closely by myopathies (n=5; 20.8%). Moreover, most AR mortalities occurred during the recovery period (n=12; 50%). When we only investigate the elective group, the most important death cause is ventricular fibrillation (n=2; 40%). In the non-elective group, myopathies is considered to be the most important death cause (n=5; 26.3%).

		Non-elective		Elective		Total	
		n	%	n	%	n	%
Causes	*Maintenance - Circulatory complications - Arrhythmia - Pathological - Ventricular - Ventricular fibrillation*	1	**5.3**	2	**40**	3	**12.5**
	Maintenance - Circulatory complications - Hypotension	3	**15.8**	-	**-**	3	**12.5**
	Maintenance - Circulatory complications - Arrhythmia - Pathological - Asystole	2	**10.5**	-	**-**	2	**8.3**
	Maintenance - Circulatory complications - Acidosis - Metabolic acidosis	1	**5.3**	-	**-**	1	**4.2**
	Recovery - Myopathy	5	**26.3**	-	**-**	5	**20.8**
	Recovery - Trauma - Muscle / Tendon tear	2	**10.5**	-	**-**	2	**8.3**
	Recovery - Circulatory complications - Cardiac arrest	1	**5.3**	-	**-**	1	**4.2**
	Recovery - Respiratory complications - Apnoea	1	**5.3**	-	**-**	1	**4.2**
	Recovery - Respiratory complications - Dyspnoea - Shortness of breath	-	**-**	1	**20**	1	**4.2**
	Recovery - Trauma - Fractures	1	**5.3**	-	**-**	1	**4.2**
	Recovery - Bleeding (without trauma) - Other	1	**5.3**	-	**-**	1	**4.2**
	Aftercare - Laminitis	1	**5.3**	1	**20**	2	**8.3**
	Aftercare - Colic	-	**-**	1	**20**	1	**4.2**
Total		**19**	100	**5**	100	**24**	100
Part of anaesthesia	*Maintenance*	7	**36.8**	2	**40**	9	**37.5**
	Recovery	11	**57.9**	1	**20**	12	**50**
	Aftercare	1	**5.3**	2	**40**	3	**12.5**

Table 24: Causes of AR mortalities.

AR morbidity incidences

As mentioned in the data description, AR morbidities are merged into larger groups for the benefit of the analysis of the influence on AR mortality. However, to determine the incidences of the different AR morbidities, the individual morbidities are shown in table 25, accompanied with their corresponding frequencies. It becomes clear that "mild" trauma (wounds, bruises, hematomas and ocular trauma including corneal erosions) are the most common AR morbidities (n=86), followed by a large group of morbidities involving the musculoskeletal system (n=44) of which the largest group consists of myopathy cases (n=21). A third place is for gastro-intestinal (colic, colitis / diarrhoea and typhlitis) morbidities (n=23).

		Elective	Non-elective	Total
AR Morbidity	*Trauma - Wound, bruise and hematoma*	28	35	**63**
	Trauma - Ocular trauma	14	9	**23**
	Musculoskeletal - Myopathy	3	18	**21**
	Musculoskeletal - Laminitis	4	4	**8**
	Musculoskeletal - Neuropathy	1	5	**6**
	Musculoskeletal - Muscle / tendon tear	-	2	**2**
	Musculoskeletal - Fractures	-	1	**1**
	Musculoskeletal - Other	3	3	**6**
	Gastro-intestinal - Colic	17	3	**20**
	Gastro-intestinal - Colitis / diarrhoea	1	1	**2**
	Gastro-intestinal - Typhlitis	1	0	**1**
	Other - Facialis paralysis	8	4	**12**
	Respiratory - Aspiration pneumonia	1	3	**4**
	Other - Thrombophlebitis	0	1	**1**
AR Morbidities	*Overall incidence*	**74** (3.2%)	**74** (9.6%)	**148** (4.8%)

Table 25: AR morbidity frequencies and the overall incidence of procedures with one or more AR morbidities.

AR mortality risk factors analyses

AR mortality risk factors

Univariate analysis

Table 26 shows all independent variables analysed for their association with AR mortality along with their degrees of freedom (d.f.) and their p-value (for elective and non-elective cases). Separately for elective and non-elective cases, all variables with a p-value < 0.4 (in bold) are used in the build-up of the multivariate logistic regression model as described in the materials and methods section.

		Elective *p-value*	*d.f.*	Non-elective *p-value*
Patient characteristics				
Age	*<1 month*	0.941	5	0.604
	1 to 5 months			

	6 to 11 months			
	12 months to 4 years			
	5 to 13 years			
	> 13 years			
Gender	*Stallion*	0.965	2	**0.355**
	Gelding			
	Mare			
Breed	*Cold blood*	**0.389**	2	**0.184**
	Warm blood			
	Thoroughbred			
Weight		**0.355**	1	**0.132**
BCS	*1*	0.800	4	**0.053**
	2			
	3			
	4			
	5			
Anaesthesia characteristics				
Procedure type	*ENT (General)*	0.963	12	0.405
	ENT (Trauma)			
	ENT (Oesophageal obstruction)			
	Genitourinary (General)			
	Genitourinary (Castration)			
	Orthopedics (General)			
	Orthopedics (Trauma)			
	Orthopedics (Fractures)			
	Colic			
	Medical imaging (General)			
	Medical imaging (CT-Standing)			
	Medical imaging (CT-GA)			
	Medical imaging (MRI-GA)			
	Others			
ASA	*1*	0.492	3 - 4	**0.000**
	2			
	3			
	4			
	5 ***(Non-elective)***			
Anaesthetist training level	*Specialist*	**0.329**	2	0.782
	Resident			
	Intern			
Anaesthesia type	*Standing sedation*	0.976	7 - 6	0.594
	General anaesthesia - inhalation (Spontaneous breathing)			
	General anaesthesia - inhalation (IPPV)			
	General anaesthesia - inhalation (IPPV + PEEP)			
	General anaesthesia - TIVA			

	Combination anaesthesia - inhalation (Spontaneous breathing) *Combination anaesthesia - inhalation (IPPV)* *Combination anaesthesia - inhalation (IPPV + PEEP)**(Elective)***			
Body position	*Standing position* *Dorsal recumbency* *Left lateral recumbency* *Right lateral recumbency*	0.670	3	**0.094**
Premedication agent(s)	*α2-Agonist* *α2-Agonist + Opioid* *Acepromazine + α2-Agonist* *Acepromazine + Opioid* *Acepromazine + α2-Agonist + Opioid* *Benzodiazepine + Opioid*	**0.033**	5	**0.171**
Induction agent(s)	*None (Standing sedation)* *Ketamine + Midazolam* *Ketamine + Diazepam* *Ketamine + Propofol* *Propofol* *Thiopental + Midazolam **(Elective)*** *Thiopental + Gujatal **(Elective)***	0.996	6 - 4	**0.347**
Maintenance agent(s)	*Isoflurane* *Isoflurane, α2-Agonist* *Isoflurane, α2-Agonist, Ketamine* *Isoflurane, Ketamine, Lidocaine* *α2-Agonist* *α2-Agonist, Ketamine, Gujatal* *Others*	0.830	7	0.420
Start time of the anaesthesia	*0:00 - 5:59* *6:00 - 11:59* *12:00 - 17:59* *18:00 - 24:00*	0.989	3	0.429
Duration of the anaesthesia		**0.189**	1	**0.165**
Day of the week	*Weekday* *Weekend*	1.000	1	0.439
Season of the year	*Jan - Mar* *Apr - Jun* *Jul - Sep* *Oct - Dec*	0.922	3	0.444
Peri-procedural complications	***Respiratory - Tachypnoea***	**0.000**	1	**0.095**
	Respiratory - Dyspnoea	**0.000**	1	**0.002**
	Respiratory - Apnoea	**0.000**	1	**0.000**
	Circulatory - Brady / Tachycardia	1.000	1	**0.002**
	Circulatory - Hypotension	1.000	1	**0.000**

	Circulatory - Hypothermia	1.000	1	**0.047**
	Circulatory - Acidosis	1.000	1	**0.008**
	Circulatory - O2 / CO2 Imbalance	1.000	1	**0.213**
	Circulatory - Electrolyte imbalance	**0.151**	1	**0.140**
	Circulatory - Pathological arrhythmia	**0.000**	1	**0.000**
	Circulatory - Other	**0.379**	1	0.637
	Problems intubation	1.000	1	**0.118**
	Problems extubation	1.000	1	1.000
	Turbulent recovery	1.000	1	0.474
	Insufficient depth of anaesthesia	0.451	1	**0.330**
	Bleeding - from trauma	1.000	1	**0.382**
	Bleeding - without trauma	1.000	1	**0.049**
	Other	1.000	1	**0.349**
AR morbidities				
Morbidities	***Musculoskeletal - Myopathy, neuropathy, laminitis, etc.***	1.000	1	**0.000**
	Musculoskeletal - Muscle / tendon tear and fractures	-	1	**0.000**
	Gastro-intestinal	**0.036**	1	1.000
	Respiratory related	1.000	1	1.000
	Trauma - Mild	1.000	1	1.000
	Other	1.000	1	1.000

Table 26: Univariate analysis of risk factors associated with the AR mortality.

Multivariate analysis

Both the elective cases and the non-elective cases did not result in a useful multivariate logistic regression model. This is due to the fact that not a single independent variable meets the condition that it significantly improves the fit of the model and is significantly associated with the AR mortality. Therefore, no table for the outcome is given.

AR morbidity risk factors analyses

Overall AR morbidity risk factors

Univariate analysis

Table 27 shows all independent variables analysed for their association with the overall AR morbidity (the development of one or more AR morbidities) along with their degrees of freedom (d.f.) and their p-value (for elective and non-elective cases). Separately for elective and non-elective cases, all variables with a p-value < 0.4 (in bold) are used in the build-up of the multivariate logistic regression model as described in the materials and methods.

		Elective *p-value*	*d.f.*	Non-elective *p-value*
Patient characteristics				
Age	*<1 month*	**0.171**	5	**0.045**
	1 to 5 months			
	6 to 11 months			

	12 months to 4 years			
	5 to 13 years			
	> 13 years			
Gender	*Stallion*	**0.275**	2	0.569
	Gelding			
	Mare			
Breed	*Cold blood*	0.721	2	**0.302**
	Warm blood			
	Thoroughbred			
Weight		**0.151**	1	**0.010**
BCS	*1*	0.903	4	0.823
	2			
	3			
	4			
	5			
Anaesthesia characteristics				
Procedure type	*ENT (General)*	**0.144**	12	**0.164**
	ENT (Trauma)			
	ENT (Oesophageal obstruction)			
	Genitourinary (General)			
	Genitourinary (Castration)			
	Orthopedics (General)			
	Orthopedics (Trauma)			
	Orthopedics (Fractures)			
	Colic			
	Medical imaging (General)			
	Medical imaging (CT-Standing)			
	Medical imaging (CT-GA)			
	Medical imaging (MRI-GA)			
	Others			
ASA	*1*	0.522	3 - 4	**0.111**
	2			
	3			
	4			
	5 ***(Non-elective)***			
Anaesthetist training level	*Specialist*	**0.051**	2	**0.335**
	Resident			
	Intern			
Anaesthesia type	*Standing sedation*	**0.124**	7 - 6	**0.021**
	General anaesthesia - inhalation (Spontaneous breathing)			
	General anaesthesia - inhalation (IPPV)			
	General anaesthesia - inhalation (IPPV + PEEP)			
	General anaesthesia - TIVA			
	Combination anaesthesia - inhalation (Spontaneous breathing)			

	Combination anaesthesia - inhalation (IPPV) *Combination anaesthesia - inhalation (IPPV + PEEP)**(Elective)***			
Body position	*Standing position* *Dorsal recumbency* *Left lateral recumbency* *Right lateral recumbency*	**0.047**	3	**0.148**
Premedication agent(s)	*α2-Agonist* *α2-Agonist + Opioid* *Acepromazine + α2-Agonist* *Acepromazine + Opioid* *Acepromazine + α2-Agonist + Opioid* *Benzodiazepine + Opioid*	**0.049**	5	**0.277**
Induction agent(s)	*None (Standing sedation)* *Ketamine + Midazolam* *Ketamine + Diazepam* *Ketamine + Propofol* *Propofol* *Thiopental + Midazolam **(Elective)*** *Thiopental + Gujatal **(Elective)***	**0.144**	6 - 4	**0.211**
Maintenance agent(s)	*Isoflurane* *Isoflurane, α2-Agonist* *Isoflurane, α2-Agonist, Ketamine* *Isoflurane, Ketamine, Lidocaine* *α2-Agonist* *α2-Agonist, Ketamine, Gujatal* *Others*	0.524	7	**0.088**
Start time of the anaesthesia	*0:00 - 5:59* *6:00 - 11:59* *12:00 - 17:59* *18:00 - 24:00*	0.646	3	0.728
Duration of the anaesthesia		**0.000**	1	**0.000**
Day of the week	*Weekday* *Weekend*	1.000	1	0.831
Season of the year	*Jan - Mar* *Apr - Jun* *Jul - Sep* *Oct - Dec*	**0.017**	3	**0.043**
Peri-procedural complications	***Respiratory - Tachypnoea***	1.000	1	**0.333**
	Respiratory - Dyspnoea	**0.026**	1	**0.061**
	Respiratory - Apnoea	1.000	1	**0.106**
	Circulatory - Brady / Tachycardia	1.000	1	0.789
	Circulatory - Hypotension	**0.063**	1	**0.250**
	Circulatory - Hypothermia	**0.002**	1	**0.001**
	Circulatory - Acidosis	1.000	1	0.641

Circulatory - O2 / CO2 Imbalance	1.000	1	**0.069**
Circulatory - Electrolyte imbalance	**0.086**	1	**0.001**
Circulatory - Pathological arrhythmia	1.000	1	0.613
Circulatory - Other	**0.176**	1	**0.022**
Problems intubation	1.000	1	**0.398**
Problems extubation	**0.151**	1	**0.026**
Turbulent recovery	**0.000**	1	**0.000**
Insufficient depth of anaesthesia	**0.001**	1	**0.022**
Bleeding - from trauma	**0.009**	1	**0.029**
Bleeding - without trauma	1.000	1	1.000
Other	**0.066**	1	**0.072**

Table 27: Univariate analysis of risk factors associated with the overall AR morbidity.

Elective cases

The multivariate logistic regression model of risk factors associated with the overall AR morbidity (the development of one or more AR morbidities), for elective cases, is statistically significant ($\chi 2 = 53.288$ - *p = 0.000*) and does not lack fit (Hosmer-Lemeshow – *p-value = 0.390*). The final logistic regression model explains 12% (Nagelkerke R^2) of the outcome variable: overall AR morbidity (elective). The model classifies 96.2% of all the cases correctly, with a sensitivity of 99.9% and a specificity of 0%. After the backward build-up procedure only 7 independent variables (predictors) remained. Four of these predictors have a significant association with the outcome (Wald statistic *p < 0.05*). The significant odds ratios of the model (p-values in bold) should be interpreted as follows. Odd ratios larger than 1 indicate a higher risk of an AR morbidity and odd ratios between 0 and 1 indicate a reduced risk of an AR morbidity. An increase in the duration of anaesthesia, results in a higher risk to develop an AR morbidity. Specifically, an increased procedure duration is associated with an odd ratio of 1.3, and thus associated with an increased risk. Season of the year on the other hand has a larger influence. Namely, the first two quarters (Jan – Mar & Apr – Jun) are associated with a risk approximately three times as high as in the third quarter (Jul - Sep). Furthermore, the strongest associations are seen for the two included peri-procedural complications, namely the presence of hypothermia and/or a turbulent recovery. All these results are shown in table 28.

		S.E.	p-value	Odds ratio	95% CI	
					Lower	*Upper*
Patient characteristics						
Gender	*Stallion*	Referent	0.08			
	Gelding	0.46	0.81	1.12	0.45	2.78
	Mare	0.43	0.11	2.01	0.86	4.68
Weight		0.00	0.08	1.00	1.00	1.00
Anaesthesia characteristics						
Anaesthetist training level	*Specialist*	Referent	0.05			
	Resident	0.47	0.30	0.61	0.24	1.55
	Intern	0.29	0.07	1.70	0.96	3.00

Duration of the anaesthesia		0.11	**0.02**	1.30	1.05	1.61
Season of the year	***Jan - Mar***	0.46	**0.01**	3.37	1.36	8.34
	Apr - Jun	0.44	**0.01**	3.42	1.43	8.14
	Jul - Sep	Referent	**0.02**			
	Oct - Dec	0.50	0.21	1.86	0.70	4.92
Peri-procedural complications	***Circulatory - Hypothermia***	0.54	**0.01**	4.36	1.52	12.51
	Turbulent recovery	0.35	**0.00**	3.61	1.84	7.09

Table 28: Multivariate logistic regression model of risk factors associated with the overall AR morbidity (Elective).

Non-elective cases

The multivariate logistic regression model of risk factors associated with the overall AR morbidity (the development of one or more AR morbidities), for non-elective cases, is statistically significant ($\chi 2$ = 81.241- *p = 0.000*) and does not lack fit (Hosmer-Lemeshow – *p-value = 0.695*). The final logistic regression model explains 22.3% (Nagelkerke R^2) of the outcome variable: overall AR morbidity (non-elective). The model classifies 90.7% of all the cases correctly, with a sensitivity of 99.5% and a specificity of 11.1%. After the backward build-up procedure only 8 independent variables (predictors) remained. Five of these predictors have a significant association with the outcome (Wald statistic *p < 0.05*). The significant odds ratios of the model (p-values in bold) should be interpreted the same as the previous logistic regression model. An increase in the duration of anaesthesia, results in a higher risk to develop an AR morbidity. Season of the year has a substantial influence as well. Namely, the second quarter (Apr – Jun) is associated with a risk approximately three times as high as in the third quarter (Jul - Sep). Furthermore, the strongest associations are seen in three of the included peri-procedural complications, namely the presence of apnoea, hypothermia and/or a turbulent recovery. All these results are shown in table 29.

		S.E.	p-value	Odds ratio	95% CI	
					Lower	*Upper*
Anaesthesia characteristics						
Maintenance agent(s)	*Isoflurane*	1.16	0.28	0.29	0.03	2.80
	Isoflurane, α2-Agonist	Referent	0.96			
	Isoflurane, α2-Agonist, Ketamine	12833.10	1.00	0.00	0.00	.
	Isoflurane, Ketamine, Lidocaine	0.30	0.63	0.87	0.48	1.55
	α2-Agonist	7645.91	1.00	0.00	0.00	.
	α2-Agonist, Ketamine, Gujatal	11740.79	1.00	0.00	0.00	.
	Others	0.46	0.54	0.75	0.31	1.86

Duration of the anaesthesia		0.14	**0.00**	1.68	1.29	2.20
Season of the year	*Jan - Mar*	0.43	0.68	1.20	0.52	2.77
	Apr - Jun	0.40	**0.00**	3.10	1.43	6.73
	Jul - Sep	Referent	**0.01**			
	Oct - Dec	0.41	0.07	2.13	0.95	4.74
Peri-procedural complications	***Respiratory - Apnoea***	1.19	**0.02**	15.50	1.51	159.14
	Circulatory - Hypotension	7580.95	1.00	0.00	0.00	.
	Circulatory - Hypothermia	0.45	**0.05**	2.44	1.00	5.96
	Problems extubation	1.25	0.09	8.11	0.71	93.35
	Turbulent recovery	0.32	**0.00**	3.93	2.11	7.33

Table 29: Multivariate logistic regression model of risk factors associated with the overall AR morbidity (Non-elective).

AR mild trauma risk factors

Univariate analysis

Table 30 shows all independent variables analysed for their association with AR mild trauma (AR morbidity nr. 1) along with their degrees of freedom (d.f.) and their p-value (for elective and non-elective cases). Separately for elective and non-elective cases, all variables with a p-value < 0.4 (in bold) are used in the build-up of the multivariate logistic regression model as described in the materials and methods.

		Elective *p-value*	*d.f.*	Non-elective *p-value*
Patient characteristics				
Age	*<1 month*	0.919	5	**0.321**
	1 to 5 months			
	6 to 11 months			
	12 months to 4 years			
	5 to 13 years			
	> 13 years			
Gender	*Stallion*	**0.098**	2	0.855
	Gelding			
	Mare			
Breed	*Cold blood*	0.962	2	0.587
	Warm blood			
	Thoroughbred			
Weight		0.894	1	**0.047**
BCS	*1*	0.924	4	0.613
	2			
	3			
	4			
	5			

Anaesthesia characteristics				
Procedure type	*ENT (General)* *ENT (Trauma)* *ENT (Oesophageal obstruction)* *Genitourinary (General)* *Genitourinary (Castration)* *Orthopedics (General)* *Orthopedics (Trauma)* *Orthopedics (Fractures)* *Colic **(Non-elective)*** *Medical imaging (General)* *Medical imaging (CT-Standing)* *Medical imaging (CT-GA)* *Medical imaging (MRI-GA)**(Elective)*** *Others*	0.435	12	**0.173**
ASA	*1* *2* *3* *4* *5 **(Non-elective)***	0.941	3 - 4	**0.099**
Anaesthetist training level	*Specialist* *Resident* *Intern*	**0.016**	2	**0.114**
Anaesthesia type	*Standing sedation* *General anaesthesia - inhalation (Spontaneous breathing)* *General anaesthesia - inhalation (IPPV)* *General anaesthesia - inhalation (IPPV + PEEP)* *General anaesthesia - TIVA* *Combination anaesthesia - inhalation (Spontaneous breathing)* *Combination anaesthesia - inhalation (IPPV)* *Combination anaesthesia - inhalation (IPPV + PEEP)**(Elective)***	**0.358**	7 - 6	**0.396**
Body position	*Standing position* *Dorsal recumbency* *Left lateral recumbency* *Right lateral recumbency*	0.613	3	**0.071**
Premedication agent(s)	*α2-Agonist* *α2-Agonist + Opioid* *Acepromazine + α2-Agonist* *Acepromazine + Opioid* *Acepromazine + α2-Agonist + Opioid* *Benzodiazepine + Opioid*	**0.367**	5	0.936
Induction agent(s)	*None (Standing sedation)* *Ketamine + Midazolam* *Ketamine + Diazepam*	0.781	6 - 4	0.499

	Ketamine + Propofol			
	Propofol			
	Thiopental + Midazolam ***(Elective)***			
	Thiopental + Gujatal ***(Elective)***			
Maintenance agent(s)	*Isoflurane*	0.992	7	**0.196**
	Isoflurane, α2-Agonist			
	Isoflurane, α2-Agonist, Ketamine			
	Isoflurane, Ketamine, Lidocaine			
	α2-Agonist			
	α2-Agonist, Ketamine, Gujatal			
	Others			
Start time of the anaesthesia	*0:00 - 5:59*	0.845	3	**0.195**
	6:00 - 11:59			
	12:00 - 17:59			
	18:00 - 24:00			
Duration of the anaesthesia		**0.145**	1	**0.001**
Day of the week	*Weekday*	1.000	1	0.671
	Weekend			
Quarter of the year (seasons)	*Jan - Mar*	**0.356**	3	**0.049**
	Apr - Jun			
	Jul - Sep			
	Oct - Dec			
Peri-procedural complications	*Respiratory - Tachypnoea*	1.000	1	1.000
	Respiratory - Dyspnoea	**0.066**	1	**0.361**
	Respiratory - Apnoea	1.000	1	1.000
	Circulatory - Brady / Tachycardia	1.000	1	0.720
	Circulatory - Hypotension	1.000	1	0.623
	Circulatory - Hypothermia	**0.039**	1	**0.108**
	Circulatory - Acidosis	1.000	1	0.533
	Circulatory - O2 / CO2 Imbalance	1.000	1	0.431
	Circulatory - Electrolyte imbalance	**0.143**	1	**0.005**
	Circulatory - Pathological arrhythmia	1.000	1	1.000
	Circulatory - Other	0.784	1	**0.207**
	Problems intubation	1.000	1	1.000
	Problems extubation	1.000	1	**0.155**
	Turbulent recovery	**0.001**	1	**0.000**
	Insufficient anaesthesia	**0.127**	1	**0.011**
	Bleeding - without trauma	1.000	1	1.000
	Other	**0.010**	1	**0.060**

Table 30: Univariate analysis of risk factors associated with AR mild trauma (AR morbidity nr. 1).

Elective cases

The multivariate logistic regression model of risk factors associated with AR mild trauma, for elective cases, is statistically significant ($\chi 2 = 35.726$ - *p = 0.000*) and does not lack fit (Hosmer-Lemeshow – *p-value = 0.247*). The final logistic regression model explains 12.7% (Nagelkerke R^2) of the outcome variable: AR mild trauma (elective). The model classifies 98.1% of all the cases correctly, with a

sensitivity of 100% and a specificity of 0%. After the backward build-up procedure only 6 independent variables (predictors) remained. Five of these predictors have a significant association with the outcome (Wald statistic *p < 0.05*). The significant odds ratios of the model (p-values in bold) should be interpreted as follows. Odd ratios larger than 1 indicate a higher risk of an AR mild trauma and odd ratios between 0 and 1 indicate a reduced risk of an AR mild trauma. Gender has a significant influence on the developing of an AR mild trauma, specifically, geldings are associated with a risk approximately three times as low as in mares. Procedures with an intern as anaesthetists are 2.41 times more likely to develop an AR mild trauma than with a specialist. Furthermore, the strongest associations are seen in the three included peri-procedural complications, namely the presence of hypothermia, a turbulent recovery and/or the "Other" complications group. All these results are shown in table 31.

		S.E.	p-value	Odds ratio	95% CI	
					Lower	*Upper*
Patient characteristics						
Gender	*Stallion*	0.56	0.12	0.42	0.14	1.24
	Gelding	0.48	**0.01**	0.30	0.12	0.77
	Mare	Referent	**0.02**			
Anaesthesia characteristics						
Anaesthetist training level	***Specialist***	Referent	**0.04**			
	Resident	0.68	0.56	0.67	0.18	2.53
	Intern	0.41	**0.03**	2.41	1.09	5.37
Premedication agent(s)	*α2-Agonist*	0.76	0.77	0.80	0.18	3.52
	α2-Agonist + Opioid	Referent	0.10			
	Acepromazine + α2-Agonist	0.82	**0.00**	11.70	2.33	58.79
	Acepromazine + Opioid	19899.80	1.00	0.00	0.00	.
	Acepromazine + α2-Agonist + Opioid	0.77	0.68	1.38	0.30	6.23
	Benzodiazepine + Opioid	9939.48	1.00	0.00	0.00	.
Peri-procedural complications	***Circulatory - Hypothermia***	0.66	**0.01**	5.52	1.52	19.96
	Turbulent recovery	0.46	**0.00**	3.74	1.52	9.23
	Other	0.68	**0.04**	4.18	1.11	15.80

Table 31: Multivariate logistic regression model of risk factors associated with AR mild trauma (Elective).

Non-elective cases

The multivariate logistic regression model of risk factors associated with AR mild trauma, for non-elective cases, is statistically significant ($\chi 2 = 55.623$ - *p = 0.000*) and does not lack fit (Hosmer-Lemeshow – *p-value = 0.808*). The final logistic regression model explains 21.3% (Nagelkerke R^2) of the outcome variable: AR mild trauma (non-elective). The model classifies 94.4% of all the cases correctly, with a sensitivity of 100% and a specificity of 0%. After the backward build-up procedure only 4 independent variables (predictors) remained. Three of these predictors have a significant association

with the outcome (Wald statistic $p < 0.05$). The significant odds ratios of the model (p-values in bold) should be interpreted the same as the previous logistic regression model. An increase in the duration of anaesthesia, results in a higher risk to develop AR mild trauma (e.g. 120 minutes, results in an odd ratio of 3.3). Season of the year has a substantial influence as well. Namely, the first and last quarter (Jan – Mar & Apr – Jun) are associated with a risk approximately three times as high as in the third quarter (Jul - Sep). Furthermore, the strongest association is seen in the included peri-procedural complication: the presence of a turbulent recovery. All these results are shown in table 32.

		S.E.	p-value	Odds ratio	95% CI	
					Lower	*Upper*
Anaesthesia characteristics						
Maintenance agent(s)	*Isoflurane*	6795.55	1.00	0.00	0.00	.
	Isoflurane, α2-Agonist	Referent	0.97			
	Isoflurane, α2-Agonist, Ketamine	12559.79	1.00	0.00	0.00	.
	Isoflurane, Ketamine, Lidocaine	0.37	0.86	0.94	0.45	1.94
	α2-Agonist	7373.09	1.00	0.00	0.00	.
	α2-Agonist, Ketamine, Gujatal	11239.72	1.00	0.00	0.00	.
	Others	0.69	0.26	0.46	0.12	1.78
Duration of the anaesthesia		0.18	**0.01**	1.64	1.15	2.33
Season of the year	***Jan - Mar***	0.50	**0.04**	2.82	1.07	7.48
	Apr - Jun	0.58	0.87	0.91	0.29	2.83
	Jul - Sep	Referent	**0.03**			
	Oct - Dec	0.50	**0.03**	2.90	1.09	7.77
Peri-procedural complications	***Turbulent recovery***	0.37	**0.00**	6.85	3.32	14.15

Table 32: Multivariate logistic regression model of risk factors associated with AR mild trauma (Non-elective).

AR myopathy risk factors

Univariate analysis

As shown before, the number 2 AR morbidity are musculoskeletal related morbidities of which the largest group consists of myopathies. Therefore, and because of the relatively broad difference of the aetiologies of the subgroups, AR myopathy is analysed solely as the second important AR morbidity in this study. Table 33 shows all independent variables analysed for their association with AR myopathy along with their degrees of freedom (d.f.) and their p-value (for elective and non-elective cases). Separately for elective and non-elective cases, all variables with a p-value < 0.4 (in bold) are used in the build-up of the multivariate logistic regression model as described in the materials and methods.

		Elective *p-value*	*d.f.*	Non-elective *p-value*
Patient characteristics				
Age	*<1 month*	**0.145**	5	**0.308**
	1 to 5 months			
	6 to 11 months			
	12 months to 4 years			
	5 to 13 years			
	> 13 years			
Gender	*Stallion*	0.468	2	**0.328**
	Gelding			
	Mare			
Breed	*Cold blood*	0.931	2	0.408
	Warm blood			
	Thoroughbred			
Weight		0.415	1	**0.010**
BCS	*1*	0.968	4	0.912
	2			
	3			
	4			
	5			
Anaesthesia characteristics				
Procedure type	*ENT (General)*	**0.245**	12	0.954
	ENT (Trauma)			
	ENT (Oesophageal obstruction)			
	Genitourinary (General)			
	Genitourinary (Castration)			
	Orthopedics (General)			
	Orthopedics (Trauma)			
	Orthopedics (Fractures)			
	*Colic **(Non-elective)***			
	Medical imaging (General)			
	Medical imaging (CT-Standing)			
	Medical imaging (CT-GA)			
	*Medical imaging (MRI-GA)**(Elective)***			
	Others			
ASA	*1*	**0.110**	3 - 4	0.763
	2			
	3			
	4			
	*5 **(Non-elective)***			
Anaesthetist training level	*Specialist*	**0.166**	2	0.986
	Resident			
	Intern			
Anaesthesia type	*Standing sedation*	**0.306**	7 - 6	**0.186**

	General anaesthesia - inhalation (Spontaneous breathing) *General anaesthesia - inhalation (IPPV)* *General anaesthesia - inhalation (IPPV + PEEP)* *General anaesthesia - TIVA* *Combination anaesthesia - inhalation (Spontaneous breathing)* *Combination anaesthesia - inhalation (IPPV)* *Combination anaesthesia - inhalation (IPPV + PEEP)**(Elective)***			
Body position	*Standing position* *Dorsal recumbency* *Left lateral recumbency* *Right lateral recumbency*	**0.047**	3	**0.041**
Premedication agent(s)	*α2-Agonist* *α2-Agonist + Opioid* *Acepromazine + α2-Agonist* *Acepromazine + Opioid* *Acepromazine + α2-Agonist + Opioid* *Benzodiazepine + Opioid*	**0.065**	5	**0.059**
Induction agent(s)	*None (Standing sedation)* *Ketamine + Midazolam* *Ketamine + Diazepam* *Ketamine + Propofol* *Propofol* *Thiopental + Midazolam **(Elective)*** *Thiopental + Gujatal **(Elective)***	**0.285**	6 - 4	**0.218**
Maintenance agent(s)	*Isoflurane* *Isoflurane, α2-Agonist* *Isoflurane, α2-Agonist, Ketamine* *Isoflurane, Ketamine, Lidocaine* *α2-Agonist* *α2-Agonist, Ketamine, Gujatal* *Others*	**0.207**	7	0.767
Start time of the anaesthesia	*0:00 - 5:59* *6:00 - 11:59* *12:00 - 17:59* *18:00 - 24:00*	0.995	3	**0.127**
Duration of the anaesthesia		**0.001**	1	**0.002**
Day of the week	*Weekday* *Weekend*	1.000	1	0.616
Season of the year	*Jan - Mar* *Apr - Jun* *Jul - Sep* *Oct - Dec*	**0.034**	3	0.505

Peri-procedural complications	***Respiratory - Tachypnoea***	1.000	1	**0.091**
	Respiratory - Dyspnoea	1.000	1	**0.098**
	Respiratory - Apnoea	1.000	1	**0.007**
	Circulatory - Brady / Tachycardia	1.000	1	0.617
	Circulatory - Hypotension	**0.003**	1	1.000
	Circulatory - Hypothermia	**0.055**	1	**0.041**
	Circulatory - Acidosis	1.000	1	1.000
	Circulatory - O2 / CO2 Imbalance	1.000	1	**0.044**
	Circulatory - Electrolyte imbalance	1.000	1	**0.209**
	Circulatory - Pathological arrhythmia	1.000	1	1.000
	Circulatory - Other	1.000	1	**0.365**
	Problems intubation	1.000	1	**0.112**
	Problems extubation	1.000	1	1.000
	Turbulent recovery	**0.153**	1	**0.012**
	Insufficient anaesthesia	**0.302**	1	**0.159**
	Bleeding - from trauma	1.000	1	**0.366**
	Bleeding - without trauma	1.000	1	1.000
	Other	1.000	1	1.000

Table 33: Univariate analysis of risk factors associated with AR myopathy (largest group of AR morbidity nr. 2: Musculoskeletal related).

Elective cases

The elective cases sample does not result in a useful multivariate logistic regression model. This is due to the fact that not a single independent variable meets the condition that it significantly improves the fit of the model and is significantly associated with AR myopathy. Therefore, no table for the outcome is given.

Non-elective cases

The multivariate logistic regression model of risk factors associated with AR myopathy, for non-elective cases, is statistically significant ($\chi 2 = 56.743$ - $p = 0.000$) and does not lack fit (Hosmer-Lemeshow – p-$value = 0.971$). The final logistic regression model explains 36.4% (Nagelkerke R^2) of the outcome variable: AR myopathy (non-elective). The model classifies 97.6% of all the cases correctly, with a sensitivity of 99.7% and a specificity of 16.7%. After the backward build-up procedure only 9 independent variables (predictors) remained. Five of these predictors have a significant association with the outcome (Wald statistic $p < 0.05$). The significant odds ratios of the model (p-values in bold) should be interpreted as follows. Odd ratios larger than 1 indicate a higher risk of an AR myopathy and odd ratios between 0 and 1 indicate a reduced risk of an AR myopathy. A higher weight of the patient is associated with a higher risk to develop an AR myopathy. Another significant variable is the body position. More specifically, a “Left lateral recumbency” is considered 13.45 times more likely to develop an AR myopathy compared to a “Dorsal recumbency”. Furthermore, an increase in the duration of the anaesthesia is also considered with a higher risk for developing an AR myopathy. However, the strongest associations are seen in two of the included peri-procedural complications, namely the presence of apnoea and/or problems with intubation. All these results are shown in table 34.

		S.E.	p-value	Odds ratio	95% CI Lower	95% CI Upper
Patient characteristics						
Weight		0.00	**0.00**	1.01	1.00	1.02
Anaesthesia characteristics						
Anaesthesia type	*Standing sedation*	7170.59	1.00	0.00	0.00	.
	General anaesthesia - inhalation (Spontaneous breathing)	1.24	0.17	5.45	0.48	62.24
	General anaesthesia - inhalation (IPPV)	Referent	0.63			
	General anaesthesia - inhalation (IPPV + PEEP)	0.66	0.08	3.16	0.87	11.42
	General anaesthesia - TIVA	17590.43	1.00	0.00	0.00	.
	Combination anaesthesia - inhalation (Spontaneous breathing)	24446.71	1.00	0.34	0.00	.
	Combination anaesthesia - inhalation (IPPV)	7317.01	1.00	0.00	0.00	.
Body position	*Standing position*	4821.52	1.00	0.00	0.00	.
	Dorsal recumbency	Referent	**0.00**			
	Left lateral recumbency	0.75	**0.00**	13.45	3.10	58.36
Start time of the anaesthesia	*0:00 - 5:59*	0.72	0.92	1.08	0.26	4.44
	6:00 - 11:59	3458.53	1.00	0.00	0.00	.
	12:00 - 17:59	Referent	0.60			
	18:00 - 24:00	0.65	0.21	0.44	0.12	1.58
Duration of the anaesthesia		0.28	**0.01**	2.08	1.20	3.60
Peri-procedural complications	*Respiratory - Tachypnea*	1.48	0.09	11.93	0.66	214.84
	Respiratory - Apnoea	1.19	**0.01**	26.29	2.56	270.13
	Problems intubation	1.42	**0.01**	42.16	2.60	683.95
	Turbulent recovery	0.61	0.07	2.96	0.90	9.73

Table 34: Multivariate logistic regression model of risk factors associated with AR myopathy (Non-elective).

AR gastro-intestinal morbidities (colic, colitis / diarrhoea and typhlitis) risk factors

Univariate analysis

Table 35 shows all independent variables analysed for their association with AR gastro-intestinal morbidities (AR morbidity nr. 3) along with their degrees of freedom (d.f.) and their p-value (for elective and non-elective cases). Separately for elective and non-elective cases, all variables with a p-

value < 0.4 (in bold) are used in the build-up of the multivariate logistic regression model as described in the materials and methods.

		Elective *p-value*	*d.f.*	Non-elective *p-value*
Patient characteristics				
Age	*<1 month*	0.426	5	0.746
	1 to 5 months			
	6 to 11 months			
	12 months to 4 years			
	5 to 13 years			
	> 13 years			
Gender	*Stallion*	**0.383**	2	**0.180**
	Gelding			
	Mare			
Breed	*Cold blood*	**0.347**	2	0.851
	Warm blood			
	Thoroughbred			
Weight		**0.385**	1	**0.320**
BCS	*1*	0.966	4	0.972
	2			
	3			
	4			
	5			
Anaesthesia characteristics				
Procedure type	*ENT (General)*	0.593	12	**0.247**
	ENT (Trauma)			
	ENT (Oesophageal obstruction)			
	Genitourinary (General)			
	Genitourinary (Castration)			
	Orthopedics (General)			
	Orthopedics (Trauma)			
	Orthopedics (Fractures)			
	*Colic **(Non-elective)***			
	Medical imaging (General)			
	Medical imaging (CT-Standing)			
	Medical imaging (CT-GA)			
	*Medical imaging (MRI-GA)**(Elective)***			
	Others			
ASA	*1*	**0.101**	3 - 4	0.581
	2			
	3			
	4			
	*5 **(Non-elective)***			
Anaesthetist training level	*Specialist*	0.664	2	**0.337**
	Resident			

	Intern			
Anaesthesia type	*Standing sedation* *General anaesthesia - inhalation (Spontaneous breathing)* *General anaesthesia - inhalation (IPPV)* *General anaesthesia - inhalation (IPPV + PEEP)* *General anaesthesia - TIVA* *Combination anaesthesia - inhalation (Spontaneous breathing)* *Combination anaesthesia - inhalation (IPPV)* *Combination anaesthesia - inhalation (IPPV + PEEP)****(Elective)***	0.728	7 - 6	0.844
Body position	*Standing position* *Dorsal recumbency* *Left lateral recumbency* *Right lateral recumbency*	**0.271**	3	0.445
Premedication agent(s)	*α2-Agonist* *α2-Agonist + Opioid* *Acepromazine + α2-Agonist* *Acepromazine + Opioid* *Acepromazine + α2-Agonist + Opioid* *Benzodiazepine + Opioid*	**0.144**	5	0.716
Induction agent(s)	*None (Standing sedation)* *Ketamine + Midazolam* *Ketamine + Diazepam* *Ketamine + Propofol* *Propofol* *Thiopental + Midazolam****(Elective)*** *Thiopental + Gujatal****(Elective)***	0.671	6 - 4	**0.169**
Maintenance agent(s)	*Isoflurane* *Isoflurane, α2-Agonist* *Isoflurane, α2-Agonist, Ketamine* *Isoflurane, Ketamine, Lidocaine* *α2-Agonist* *α2-Agonist, Ketamine, Gujatal* *Others*	0.663	7	0.691
Start time of the anaesthesia	*0:00 - 5:59* *6:00 - 11:59* *12:00 - 17:59* *18:00 - 24:00*	0.742	3	0.617
Duration of the anaesthesia		**0.090**	1	0.542
Day of the week	*Weekday* *Weekend*	1.000	1	0.581
Season of the year	*Jan - Mar* *Apr - Jun* *Jul - Sep*	**0.060**	3	**0.109**

	Oct - Dec			
Peri-procedural complications	*Respiratory - Tachypnoea*	1.000	1	1.000
	Respiratory - Dyspnoea	**0.328**	1	1.000
	Respiratory - Apnoea	1.000	1	1.000
	Circulatory - Brady / Tachycardia	1.000	1	**0.197**
	Circulatory - Hypotension	1.000	1	1.000
	Circulatory - Hypothermia	**0.039**	1	1.000
	Circulatory - Acidosis	1.000	1	**0.257**
	Circulatory - O2 / CO2 Imbalance	1.000	1	1.000
	Circulatory - Electrolyte imbalance	**0.101**	1	0.612
	Circulatory - Pathological arrhythmia	1.000	1	1.000
	Circulatory - Other	0.663	1	1.000
	Problems intubation	1.000	1	1.000
	Problems extubation	1.000	1	1.000
	Turbulent recovery	**0.002**	1	1.000
	Insufficient depth of anaesthesia	**0.116**	1	1.000
	Bleeding - from trauma	1.000	1	1.000
	Bleeding - without trauma	1.000	1	1.000
	Other	1.000	1	1.000

Table 35: Univariate analysis of risk factors associated with AR gastro-intestinal morbidities (AR morbidity nr. 3).

Elective cases

The multivariate logistic regression model of risk factors associated with AR gastro-intestinal morbidities, for elective cases, is statistically significant ($\chi 2 = 31.940$ - *p = 0.002*) and does not lack fit (Hosmer-Lemeshow – *p-value = 0.954*). The final logistic regression model explains 20.7% (Nagelkerke R^2) of the outcome variable: AR gastro-intestinal morbidities (elective). The model classifies 99.1% of all the cases correctly, with a sensitivity of 100% and a specificity of 0%. After the backward build-up procedure only 5 independent variables (predictors) remained. Two of these predictors have a significant association with the outcome (Wald statistic *p < 0.05*). The significant odds ratios of the model (p-values in bold) should be interpreted as follows. Odd ratios larger than 1 indicate a higher risk of an AR gastro-intestinal morbidity and odd ratios between 0 and 1 indicate a reduced risk of an AR gastro-intestinal morbidity. The significant associations are seen in two of the included peri-procedural complications, namely the presence of hypothermia and/or a turbulent recovery. All these results are shown in table 36.

		S.E.	p-value	Odds ratio	95% CI	
					Lower	*Upper*
Patient characteristics						
Gender	*Stallion*	Referent	0.57			
	Gelding	2086.45	0.99	10689781.81	0.00	.
	Mare	2086.45	0.99	19425626.38	0.00	.
Breed	*Cold blood*	0.79	0.11	0.28	0.06	1.31
	Warm blood	Referent	0.11			
	Thoroughbred	1.12	0.24	3.74	0.42	33.30
Anaesthesia characteristics						

Season of the year	*Jan - Mar*	1.18	0.23	4.08	0.40	41.33
	Apr - Jun	1.10	**0.03**	11.13	1.29	96.12
	Jul - Sep	Referent	0.05			
	Oct - Dec	1.25	0.54	2.14	0.18	24.74
Peri-procedural complications	***Circulatory - Hypothermia***	0.85	**0.02**	6.81	1.28	36.33
	Turbulent recovery	0.60	**0.00**	6.92	2.14	22.37

Table 36: Multivariate logistic regression model of risk factors associated with AR gastro-intestinal morbidities (Elective).

Non-elective cases

The non-elective cases sample does not result in a useful multivariate logistic regression model. This is due to the fact that not a single independent variable meets the condition that it significantly improves the fit of the model and is significantly associated with AR gastro-intestinal morbidities. Therefore, no table for the outcome is given.

Discussion

This study examined the anaesthesia-related mortality and morbidity risk for the Department of Equine Sciences at Utrecht University, and which underlying factors influenced them. In addition, the study investigates whether the AR mortality and morbidity risk decreased in the past years, compared to previous analyses in our own clinic and to internationally reported percentages. The elective AR mortality and morbidity rate, for either surgical procedures alone or combined with diagnostic procedures, under general anaesthesia, in this study are 0.2% and 3.8%, respectively. Comparing the AR mortality rate to percentages found in a previous analyses in our own clinic and to internationally reported percentages, shows a decreased AR mortality risk for elective cases under general anaesthesia, over the past years and a lower mortality AR mortality risk for elective cases under general anaesthesia, compared to internationally reported percentages. This confirms the following two hypotheses:

- *The AR mortality risk for elective cases under general anaesthesia decreased in the past years.*
- *The AR mortality risk for elective cases under general anaesthesia is lower compared to internationally reported percentages.*

The AR morbidity for elective cases under general anaesthesia found in this study lies in between a range of internationally reported percentages. Therefore, the following two hypotheses are rejected:

- *The AR morbidity risk for elective cases under general anaesthesia decreased in the past years.*
- *The AR morbidity risk for elective cases under general anaesthesia is lower compared to internationally reported percentages.*

All results, including the answers to the research questions, are discussed in more detail in the sub-chapters below.

AR mortality

Overall (elective and non-elective cases)

The combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) overall (elective and non-elective cases) AR mortality found in this study is 0.8%. For the benefit of cross-study comparison, the combined overall group is divided into four categories, namely: general anaesthesia (with two subgroups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic). The overall (elective and non-elective cases) AR mortality found in the general anaesthesia group was 1.0%, and in the surgical and diagnostic subgroup 1.1% and 0%, respectively. The overall (elective and non-elective cases) AR mortality found in the standing sedation group was 0.3%, and in the surgical and diagnostic subgroup 0.5% and 0%, respectively.

When our results are compared with other studies, an AR mortality of 1.0% is used, while most other studies only analyse general anaesthesia's (either surgical cases alone or combined with diagnostic cases).

The overall AR mortality for general anaesthesia in this study (1.0%) is considerably lower than was found in the larger prospective multicentre studies (1.6–1.9%)(Johnston, Taylor et al. 1995, Johnston, Eastment et al. 2002, Johnston, Eastment et al. 2004). The difference in findings can be explained by several reasons. Firstly, when comparing the overall (elective and non-elective) results, possible differences in the distribution of elective/non-elective cases could lead to large differences between the overall AR mortality rates. Secondly, the development of anaesthesia methods and technology decreased the risks for patients by better preventing complications and because of increased capability of intervening in time in case of complications. Furthermore, surgical methods and technologies also developed, which could result in the decreasing of anaesthesia duration and in a shift to standing

procedures where patients previously had to undergo general anaesthesia. However, this technological development also leads to more complex surgical interventions (often with a long anaesthesia duration), which in turn could result in an increased AR mortality risk. Another explanation could concern the difference in research population. Most other studies concerning these topics are performed in the UK or USA, where the composition of breeds (mostly thoroughbred) differs from that of the Netherlands (mostly warm blood). Furthermore, the difference between this hospital and hospitals in other studies, regarding the composition of different performed procedures and the available equipment, could also be a part of the explanation. Moreover, this study was performed at a larger university clinic, whereas the multicentre studies also could contain smaller, less specialized, and less equipped clinics. Finally, there are large differences in the used methods and definitions across the different studies. An important difference is the included anaesthesia's. Most studies only include patients undergoing general anaesthesia. However, as discussed earlier, changes in surgical techniques made the shifting possible from general anaesthesia to more standing procedures. This could conceal the "total" change in AR mortality, because of the inability to compare the overall AR mortality due to the lack of reported overall AR mortalities in the past. Another important difference in methods and definitions is the interval period whereafter the outcome gets determined. In this study (and others) a 7-day interval is used, while some studies determine their outcome after only 72 hours. This could result in a lower AR mortality due to the excluding of more lingering AR mortalities.
When compared to a more recent study (1.1%)(Dugdale, Obhrai et al. 2016), we still see a lower AR mortality rate, however the difference is much smaller. This difference can also be explained by most of the above discussed reasons. Some studies found lower AR mortality rates. One of those found an overall AR mortality rate of 0.24% (Bidwell, Bramlage et al. 2007). Again, these differences can be explained by all previous reasons. However, one important difference is the median duration of anaesthesia, which is much lower (less than 1 hour) than the median duration of anaesthesia in this study (1 hour and 40 minutes). Furthermore, the study argues their population consists mostly of healthy horses (no exact distribution is given), which suggest leading to a lower AR mortality.
In comparison to a previously performed (unpublished) study at our clinic (van Erp 2017), we can see a decrease over time in the overall AR mortality (1.79%). Though there are also large differences between the previously performed study and the current study, the different methods used among the studies do not account for the difference between the overall AR mortality rate. In fact, some of these differences in methods made the difference in AR mortality rates smaller. The data collection, specifically the number of deaths, is gathered using search profiles on *Vetware*. This probably resulted in an underreporting, while the patient files often lack the correct "death status" (which has a default setting of "Alive"), which was used to determine which horses died due to the anaesthesia. On the other hand, they did not restrict the outcome interval to 7 days post anaesthesia but expended it to the patient's release from the clinic. However as many other studies suggested, the outcome interval of 7 days is long enough, ensuring that more lingering AR mortalities are included, and not too long, as this increases the uncertainty of the relation between mortality and the anaesthesia (Johnston 1993). Therefore, this could result in an increased AR mortality which in turn can contribute to the difference in AR mortality rates, however it is unlikely this alone could explain this rather large difference.

Elective

When the elective procedures are analysed separately, a combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective AR mortality rate of 0.2% is found. For the benefit of cross-study comparison, the combined elective group is also divided into the four categories, namely: general anaesthesia (with two subgroups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic). The elective AR mortality found in the general anaesthesia group was 0.2%, and in the surgical and diagnostic subgroup 0.2% and 0%, respectively. The elective AR mortality found in the standing sedation group was 0.3%, and in the surgical and diagnostic subgroup 0.6% and 0%, respectively.

The rather high elective AR mortality in the standing sedation - surgical group stands out in these statistics. However, when considering the small size of the included cases in the group (n = 522) together with the low incidence of the outcome (n = 3), this AR mortality is rather unlikely to be representative for elective surgical standing sedations in general. One of these horses was a 21 years old Friesian mare that suffered from ventricular extra systole (ASA = 3). The horse was admitted for an enucleation of the right eye. The surgery was successful, despite the occurrence of the following peri-procedural complications: Insufficient depth of anaesthesia during the premedication and the maintenance and the multiple occurrences of ventricular extra systoles during maintenance and the recovery. However, six days after surgery the horse developed laminitis. Within a day the laminitis progressed to such severity the horse had to be euthanised. The second horse was a healthy (ASA = 1) three years old Friesian cryptorchid stallion who came for a laparoscopic castration. The surgery was successful and went without any peri-procedural complications. However, the next day the horse developed colic symptoms. This progressed during the next two days (day three after surgery) into a horse that was uncomfortable in such a way (gastric reflux, pain) that it had to be euthanized. Autopsy found evidence for an endotoxemia. However, due to the highly autolytic state of the carcass, the interpretation of the found lesions were difficult. The last horse was a seven years old coldblooded gelding who came for a laparoscopic nephrectomy (ASA = 3). During surgery the following peri-procedural complications occurred: hypertension, hypochloraemia, sinus arrythmia, second degree AV block and tachypnoea during the maintenance. After the horse made a sudden jump and fell on its left side the tachypnoea worsened and evolved in periods of apnoea combined with gasping. At that moment the horse had ventricular fibrillation which eventually led to its death.

The elective AR mortality for general anaesthesia in this study (0.2%) is again considerably lower than those found in the larger prospective multicentre studies (0.9%)(Johnston, Taylor et al. 1995, Johnston, Eastment et al. 2002).

This same difference is seen when it was compared to the more recent studies (0.9%)(Jago, Corletto et al. 2015, Dugdale, Obhrai et al. 2016). If we compare the results of the current study to the previously performed study at our clinic (van Erp 2017), we again see a reduction in the AR mortality rate (0.84%).

Again, this difference in AR mortality rates can be explained by the differences in methods and definitions among the studies, diversity of the associated hospitals (e.g. available equipment, composition of performed procedures, etc.), diversity of the research population, development of surgical methods/technology and of course the possible improvement of our anaesthesia methods/technology themselves.

Non-elective

At last the non-elective procedures are analysed separately. This study found a combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) AR mortality of 2.5%, which is also considerably lower than those found in most other studies (3.8-5.4%)(Johnston, Taylor et al. 1995, Mee, Cripps et al. 1998b). When compared with a more recent study (1.6%)(Dugdale, Obhrai et al. 2016), the AR mortality rate for non-elective cases in the current study appears to be higher. However, their outcome was determined the moment the patient left the recovery box. As the data in the current study suggests, 94.7% of all non-elective AR mortalities (87.5% for the overall AR mortalities) occur during maintenance or the recovery. Thus, only 5.3% of the non-elective AR mortalities occur during the aftercare. Therefore, excluding all patients who died (or were euthanized) after leaving the recovery could result in a slightly lower AR mortality rate. However, it is unlikely this alone could explain this rather large difference. The study sample used by *Dugdale, Obhrai et al.* in 2016 is rather small (n = 1416) and could therefore lead to an unreliable mortality rate compared to those found in larger (multi-centre) studies.

When the results for the non-elective group are compared to the previously performed study at our clinic (van Erp 2017), we again see a reduction in the AR mortality rate (5.18%). A specific reason for this rather large difference is the contrast in the definition of non-elective cases, where the current

study considers all emergency procedures as non-elective, the older study only looks at the emergency abdominal surgeries (who often result in higher AR mortality rates).
Other reasons for the contrast in non-elective AR mortality rates can again be explained by the differences in methods and definitions among the studies, diversity of the associated hospitals (e.g. available equipment, composition of performed procedures, etc.), diversity of the research population, development of surgical methods/technology and of course the possible improvement of our anaesthesia methods/technology themselves.

AR mortality causes

The AR death causes, with their corresponding relative incidences, are somewhat comparable to the results described in previous studies. The top four combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) overall (elective and non-elective cases) AR mortality causes found are: cardiac arrest or cardiovascular collapse (41.7%), post-anaesthetic lameness (41.6%), respiratory complications (8.4%) and gastro-intestinal related complications (4.2%). Other studies found post-anaesthetic lameness as the most common AR death cause, namely in 34-52.4% of the AR deaths (Johnston, Eastment et al. 2004, Bidwell, Bramlage et al. 2007). This is followed by cardiac arrest or cardiovascular collapse, namely in 32-47.6% of the AR deaths (Johnston, Eastment et al. 2004, Bidwell, Bramlage et al. 2007). Furthermore, 13% of the AR deaths are the result of gastro-intestinal related complications and 4% of the AR deaths are accounted by respiratory complications (Johnston, Eastment et al. 2004). The two most common AR death causes, are in terms of relative incidence quite similar. Number three and four differ in other studies compared to the current study, meaning the death causes have swapped in rank.
Furthermore, when looking more closely into the separate different post-anaesthetic lameness cases a large difference between the AR deaths accounted by fractures (4.2% of all AR death causes) and myopathies (20.8% of all AR death causes) is found. Specifically, other studies found 23-38.1% of the AR deaths are caused by fractures and 7% are caused by myopathies. These large differences could be explained by the difference among study populations. Specifically, the relatively lightweight and temperamental thoroughbred horses in the UK/USA studies, and the relatively heavy and slightly calmer warm blood horses in the current study (Netherlands). For instance, it could be suggested that a more excitable horse is more likely to end up in a more turbulent recovery which increases the risk of AR fractures. On the other hand, warmblood horses with a higher bodyweight have a higher risk to develop an AR myopathy (as shown in this current study, which will be discussed further on).
When the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) AR mortality causes were described for the elective cases separately, another study (Johnston, Eastment et al. 2002) found relative incidences almost the same to the relative incidences they found regarding all procedure types (overall). The results found in this study differ a bit more, where cardiac arrest or cardiovascular collapse, post-anaesthetic lameness, gastro-intestinal related complications and respiratory complications have a relative incidence of 40%, 20%, 20% and 20%, respectively. However, the rather small sample size (n=2305) together with the very low incidence of AR mortalities (n=5) in the elective group, cause a rather unreliable incidence distribution compared to the other study describing these elective AR mortality causes.

AR mortality risk factors

Unfortunately we were not able to produce useful multivariate logistic regression models. The main reason for this is the rather small study sample together with the low incidence of outcome (AR mortalities). Because of the low incidence of the outcome variable, a much larger study sample would be needed in order to obtain significant predictors along with their corresponding odds ratios. However, if we compare the univariate analysis of risk factors associated with the AR mortality we can see few similarities, but no conventional analysed risk factors resulted in p-values as significant as found in other studies (Mee, Cripps et al. 1998, Johnston, Eastment et al. 2002). More interestingly, despite the small study sample and low incidence of outcome, this study found reasonable associations

to AR mortality for various peri-procedural complications and some AR morbidities as predictors, of which most have not been described/analysed before (e.g. electrolyte imbalance). However, as explained above it was not possible to produce useful multivariate regression models. Yet, with a larger research population these peri-procedural complications and AR morbidities might have a significant influence on the outcome.

AR morbidity

AR morbidity incidences

The combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) overall (elective and non-elective cases) AR morbidity found in this study is 4.8%. For the benefit of cross-study comparison, the combined overall group is divided into four categories, namely: general anaesthesia (with two subgroups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic). The overall (elective and non-elective cases) AR morbidity found in the general anaesthesia group was 6.0%, and in the surgical and diagnostic subgroup 6.2% and 3.6%, respectively. The overall (elective and non-elective cases) AR morbidity found in the standing sedation group was 2.5%, and in the surgical and diagnostic subgroup 3.4% and 1.6%, respectively.

When our results are compared with *Johnston, Eastment et al. 2004*, an AR morbidity (surgical procedures under general anaesthesia) of 6.2% is used, while their study only analysed surgical cases undergoing general anaesthesia's. *Johnston, Eastment et al. 2004* found an overall AR morbidity of 2.7% which seems considerably lower than the AR morbidity of 6.2% found in the current study. Again, possible differences in the distribution of elective/non-elective cases could lead to large differences between the overall AR morbidity rates. Another part of the difference in AR morbidity risk between these studies can be explained by the difference in the used definition for AR morbidity. The current study includes all morbidities caused by the anaesthesia as AR morbidities, were *Johnston, Eastment et al. 2004* only includes the non-fatal morbidities.

The combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective AR morbidity found in this study is 3.2%. For the benefit of cross-study comparison, the combined elective group is also divided into four categories, namely: general anaesthesia (with two subgroups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic). The elective AR morbidity found in the general anaesthesia group was 3.8%, and in the surgical and diagnostic subgroup 3.8% and 3.8%, respectively. The elective AR morbidity found in the standing sedation group was 2.5%, and in the surgical and diagnostic subgroup 3.3% and 1.6%, respectively.

When our elective results are compared with other studies, an AR morbidity (surgical procedures under general anaesthesia) of 3.8% is used, while most other studies only analyse elective general anaesthesia's (either surgical procedures alone or together with procedures cases). The elective AR morbidity rate of 3.8% found in this study, lies in between the range found in other studies (1.4-15.8%)(Young, Taylor 1993, Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015). Only the *Young, Taylor 1993* study found a lower elective AR morbidity (1.4%) than the AR morbidity found in the current study. This difference again be explained by the difference in the used definition for AR morbidity. The current study includes all morbidities caused by the anaesthesia as AR morbidities, where *Young, Taylor 1993* only includes the "serious anaesthetic-related problems".

Furthermore, when looking to the relative incidences of the different AR morbidities, one large difference stands out. Specifically, the largest fraction (58%) of the AR morbidities in the current study consists of mild traumas (wounds, bruises, hematomas and ocular trauma including corneal erosions). Other studies that describe the distribution of the different AR morbidities found a much lower incidence (4.3-6%) of these mild traumas (Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015). This clear difference in the incidence of mild trauma is probably caused by used definition of mild traumas.

And to be fair, this study defined a large number of mild traumas of which their clinical relevance is questionable, because of the relatively small impact on the wellbeing of the patients.

The distribution of the different AR morbidities varies a lot between different studies, as discussed in the background of the study. However, the most frequent AR morbidities identified in this study: mild trauma, morbidities involving the musculoskeletal system (of which the largest group consists of myopathy cases) and gastro-intestinal (colic, colitis / diarrhoea and typhlitis) morbidities, are all found to be the most important AR morbidities in the other studies (Young, Taylor 1993, Johnston, Eastment et al. 2004, Senior, Pinchbeck et al. 2007, Jago, Corletto et al. 2015).

Overall AR morbidity risk factors

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures four risk factors showed a significant association with the development of one or more AR morbidities (overall AR morbidity), specifically: duration of the anaesthesia, season of the year, hypothermia and a turbulent recovery. An increasing duration of anaesthesia increases the risk of developing one or more AR morbidities. Season of the year showed an increased risk for the first two quarters of the year compared to the third quarter. Furthermore, the occurrence of hypothermia during the anaesthesia and a turbulent recovery, both resulted in an increased risk for the development of one or more AR morbidities.

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures five risk factors showed a significant association with the development of one or more AR morbidities, specifically: duration of the anaesthesia, season of the year, periods of apnoea (during induction and/or recovery), hypothermia and a turbulent recovery. An increasing duration of anaesthesia increases the risk of developing one or more AR morbidities. Season of the year showed an increased risk for the second quarter of the year compared to the third quarter. Furthermore, the occurrence of hypothermia during the anaesthesia, periods of apnoea and a turbulent recovery, all resulted in an increased risk for the development of one or more AR morbidities.

Possible explanations for the significant predictors found, for both the elective and non-elective cases, mostly depend on the specific AR morbidity. Therefore, these explanations are given below, in the specific AR morbidities discussion section. Unfortunately, we cannot compare the overall AR morbidity (the development of one or more AR morbidities) risk factors found in the current study with other studies, because of the lack of these analyses in other studies. As mentioned in the introduction of the current study, there are few studies regarding risk factors for AR morbidities of which none assessed the overall risk factors. Although determining risk factors for the separate AR morbidities is important, analysing predictors for overall AR morbidities can be useful in the determination of important overarching risk factors.

AR mild trauma risk factors

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures five risk factors showed a significant association with the development of an AR mild trauma, specifically: gender of the patient, anaesthetist training level, hypothermia, a turbulent recovery and the “Other” group of peri-procedure complications (combined group of low incidence multiple peri-procedure complications). Gender seems to be a significant predictor on the development of an AR mild trauma, specifically, mares showed an increased risk to develop an AR mild trauma compared to geldings. The difference in risk to develop an AR mild trauma between the genders has not been described in other literature before. Perhaps the behaviour/temper varies between the different gender groups in general, which might be associated with a higher risk to develop an AR mild trauma. However, to my knowledge, there is no literature available to support that theory. The training level of the anaesthetist showed an increased risk for the procedures with interns

as the responsible anaesthetist compared to procedures with specialist anaesthetists. This could be attributed to the fact that interns have less experience as anaesthetist. Furthermore, in practice "high risk" patients are often anaesthetised by (or under the supervision of) a specialist, which likely results in a higher incidence of AR morbidities with specialists. However, the opposite appears to be true in the case of AR mild traumas.
Furthermore, the occurrence of hypothermia during the anaesthesia, a turbulent recovery and peri-procedure complications from the "Other" group, all resulted in an increased risk for the development of an AR mild trauma.
Of these peri-procedure complications, a turbulent recovery can be expected as a predictor of an AR mild trauma.
Hypothermia results in a decreasing metabolism, which in turn can result in a prolonged effect of the anaesthesia agents. The prolonged effect of the anaesthesia agents will be of influence on the duration and quality of the recovery, which can also result in an increased risk of mild traumas.
The "Other" group consists of low incidence multiple peri-procedure complications. It is difficult to give a specific explanation for this group as a predictor, because the complications inside of it are clinically very different.

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures three risk factors showed a significant association with the development of an AR mild trauma, specifically: duration of the anaesthesia, season of the year and a turbulent recovery. An increasing duration of anaesthesia increases the risk of developing an AR mild trauma. An important explanation for this finding lies in the fact that the peripheral blood flow is less in horses that are anaesthetised, which in time can result to some extent of muscle damage (myopathy), as found and described in previous performed studies (Richey, Holland et al. 1990, Franci, Leece et al. 2006, Dugdale, Obhrai et al. 2016). A myopathy could in turn lead to a more unstable patient, increasing the risk to develop a mild trauma.
Season of the year showed an increased risk for the first and last quarter of the year compared to the third quarter. This increased risk could partly be explained due to the "foal season", which could start in the first quarter and continues through the entire second quarter. Mares that undergo anaesthesia for dystocia (either for assisted vaginal extraction or for C-section) have an increased anaesthetic risk. Therefore, it could be reasonable that these quarters result in a higher incidence of AR mild trauma. However, when analysing the data it appears that dystocia procedures result in (relative and absolute) low incidences of AR mild traumas during the year and therefore has no significant influence on the difference between the quarters. Moreover, the data showed a considerable change in the (relative and absolute) incidence of AR mild traumas during the first and last quarter in colic surgeries. The reason for this uneven distribution of AR mild traumas between the quarters of the year in colic procedures is unclear.
Furthermore, the occurrence of a turbulent recovery resulted in an increased risk for the development of an AR mild trauma. As discussed before a turbulent recovery can be expected as a predictor of an AR mild trauma.

AR myopathy risk factors

Unfortunately we were not able to produce a useful multivariate logistic regression model for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures analysing AR myopathy as outcome variable. Main reason is the rather small sample size of this analysed group together with the very low incidence of outcome (n=3; 0.13%). Because of the low incidence of the outcome variable, a much larger study sample is necessary in order to obtain significant predictors along with their corresponding odds ratios.

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures five risk factors showed a significant association with the

development of an AR myopathy, specifically: body weight of the patient, body position, duration of the anaesthesia, periods of apnoea (during induction and/or recovery) and problems regarding the intubation.
Body weight of the patient showed a positive correlation with the risk of developing an AR myopathy. This can be explained by the increasing pressure on the different muscle groups in contact with the operating table (depending on the body position of the patient). Due to this higher pressure, the peripheral blood flow is compromised more, which will eventually lead to hypoxia in the muscles and consequently muscle ischemia and myopathy.
As briefly mentioned in the explanation above, body position is of significant influence on the development of AR myopathies. As you can probably imagine it determines which muscle groups are affected. Furthermore, this data suggests that left lateral recumbencies lead to a much higher risk to develop an AR myopathy then a dorsal recumbency.
An increasing duration of anaesthesia increases the risk of developing an AR myopathy (Richey, Holland et al. 1990, Franci, Leece et al. 2006, Dugdale, Obhrai et al. 2016). As explained before, the longer the anaesthesia takes, the more muscle damage can occur due to the compromised peripheral blood flow that results in hypoxia in the muscles and consequent muscle ischemia and myopathy.
The body weight of the patient and the duration of the anaesthesia showed similar positive correlations with the risk of developing an AR myopathy, while they both result in a more compromised peripheral blood flow. Due to the fact that both factors can increase the risk for myopathy, the interaction term of the body weight of the patient and the duration of the anaesthesia was analysed. Not surprisingly, this also resulted in a significant risk factor. However, the fit of the model decreased when the interaction term was included (this excludes the separate body weight and duration of the anaesthesia variables). This can be explained by the fact that the interaction term does not take into account the increased risk of a patient with a high body weight during short-term anaesthesia's. Due to the decreased fit of the model, we excluded this interaction term from the final multivariate logistic regression model.
Finally, periods of apnoea (during induction and/or recovery) and problems regarding the intubation, both led to an increased risk for the development of AR myopathy. Both can cause hypoxemia which could lead to hypoxia in muscles among other tissues. The data even suggest that problems regarding the intubation leads up to a risk approximately 42 times as high. However, when analysing the data more in dept, it appears that there is only one case of an AR myopathy, where problems regarding the intubation (a few failed blind intubation attempts resulting in a swollen pharynx) occurred. Therefore, the relevance of this finding is questionable.
Somewhat in line with our findings, a study dating back to 1990 performed univariable analyses and found hypotension during anaesthesia and a prolonged duration of anaesthesia, both resulting in an increased risk for developing AR myopathy (Richey, Holland et al. 1990). The current study showed hypotension to be of high significant value when analysed as a univariable in the elective sample only. However, as mentioned before, we were unable to produce a useful multivariate logistic regression model for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures analysing AR myopathy as outcome variable.

AR gastro-intestinal morbidities (colic, colitis / diarrhoea and typhlitis) risk factors

For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures two risk factors showed a significant association with the development of an AR gastro-intestinal morbidity (colic, colitis / diarrhoea and typhlitis), specifically: hypothermia and a turbulent recovery. The occurrence of hypothermia during the anaesthesia might be associated with an increased risk for the development of AR abdominal related morbidities. A study dating from 2013 (Nelson, Lordan et al. 2013) also found that a lower post anaesthetic rectal temperature (hypothermia) resulted in an increased risk for gastrointestinal dysfunction. Unfortunately, they gave no possible explanation for this. However, decreasing body temperature could lead to reduced

splanchnic perfusion, which in its turn can result in a decreased intestinal motility (e.g. impaction or post-operative ileus).
Furthermore, a turbulent recovery is associated with an increased risk of AR gastro-intestinal morbidities. Stress and excitation due to the turbulent recovery might also lead to decreased splanchnic perfusion. This decreased splanchnic perfusion may result in a decreased intestinal motility, which eventually could lead to an AR gastro-intestinal morbidity.
Other studies that performed multivariate logistic regressions investigating the risk factors for AR gastro-intestinal morbidities found, besides the post-operative rectal temperature, the following risk factors to be of significant influence: breed, body position, peri-operative administration of sodium benzylpenicillin, peri-operative administration of butorphanol, arterial lactate levels and hours to passage of faeces (Nelson, Lordan et al. 2013, Jago, Corletto et al. 2015).

Unfortunately, we were not able to produce a useful multivariate logistic regression model for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures analysing AR gastro-intestinal morbidities as outcome variable. Main reason is the rather small sample size of this analysed group together with the very low incidence of outcome (n=4; 0.52%). Moreover, it is nearly impossible to differentiate gastro-intestinal morbidities from underlying disease against the ones that are pure anaesthesia related, in the colic procedures group (which comprises the vast majority of the non-elective group; 66.1%). Therefore, AR gastro-intestinal morbidity incidence in the non-elective sample is relatively small. Because of the low incidence of the outcome variable, a much larger study sample is necessary in order to obtain significant predictors along with their corresponding odds ratios.

Conclusions and recommendations

In conclusion, the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) overall (elective and non-elective cases) AR mortality and morbidity rate for the Department of Equine Sciences at Utrecht University are 0.8% and 4.8%, respectively. For the benefit of cross-study comparison, the combined overall group is divided into four categories, namely: general anaesthesia (with two sub groups: surgical and diagnostic) and standing sedations (with two sub groups: surgical and diagnostic).
The overall (elective and non-elective cases) AR mortality found in the general anaesthesia group was 1.0%, and in the surgical and diagnostic subgroup 1.1% and 0%, respectively. The overall (elective and non-elective cases) AR mortality found in the standing sedation group was 0.3%, and in the surgical and diagnostic subgroup 0.5% and 0%, respectively.
The overall (elective and non-elective cases) AR morbidity found in the general anaesthesia group was 6.0%, and in the surgical and diagnostic subgroup 6.2% and 3.6%, respectively. The overall (elective and non-elective cases) AR morbidity found in the standing sedation group was 2.5%, and in the surgical and diagnostic subgroup 3.4% and 1.6%, respectively.

For combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective cases, the AR mortality and morbidity rate decrease to 0.2% and 3.2%, respectively. Similar to the overall group, the same four categories are used to divide the elective group.
The elective AR mortality found in the general anaesthesia group was 0.2%, and in the surgical and diagnostic subgroup 0.2% and 0%, respectively. The elective AR mortality found in the standing sedation group was 0.3%, and in the surgical and diagnostic subgroup 0.6% and 0%, respectively.
The elective AR morbidity found in the general anaesthesia group was 3.8%, and in the surgical and diagnostic subgroup 3.8% and 3.8%, respectively. The elective AR morbidity found in the standing sedation group was 2.5%, and in the surgical and diagnostic subgroup 3.3% and 1.6%, respectively.

For combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective cases, the AR mortality and morbidity percentages increase to 2.5% and 9.6%, respectively. Unlike the overall and elective group, the non-elective group was not divided in the four different categories, while the general anaesthesia's with surgical purposes comprises the vast majority (92.7%) of the non-elective group.

This study furthermore showed significant risk factors (using multivariate analyses) for some of the analysed outcome variables. Specifically, for the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures the current study showed significant risk factors associated with the overall AR morbidity (the development of one or more AR morbidities) and with two of the three most frequent AR morbidities identified in this study (AR mild trauma and AR gastro-intestinal morbidities). Analysing the AR myopathy in the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) elective procedures group, did not result in significant associated risk factors, due to the rather small sample size of this analysed group together with the very low incidence of outcome (n=3; 0.13%). Firstly, the following risk factors showed a significant association with overall AR morbidity (the development of one or more AR morbidities): duration of the anaesthesia, season of the year, hypothermia and a turbulent recovery. Secondly, the following risk factors showed a significant association with AR mild trauma: gender of the patient, anaesthetist training level, hypothermia, a turbulent recovery and the "Other" group of peri-procedure complications (combined group of low incidence multiple peri-procedure complications). Finally, hypothermia and a turbulent recovery are risk factors significantly associated with AR gastro-intestinal morbidities (colic, colitis / diarrhoea and typhlitis).
For the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures the current study showed significant risk factors associated with

the overall AR morbidity (the development of one or more AR morbidities) and with two of the three most frequent AR morbidities identified in this study (AR mild trauma and AR myopathy). Analysing the AR gastro-intestinal morbidities in the combined (surgical and diagnostic procedures under general anaesthesia or during standing sedations) non-elective procedures group, did not result in significant associated risk factors, due to the rather small sample size of this analysed group together with the very low incidence of outcome (n=4; 0.52%). Moreover, this low incidence of AR gastro-intestinal morbidities, is caused by the extreme difficulty encountered when trying to differentiate gastro-intestinal morbidities from underlying disease against the ones that are pure anaesthesia related, in the colic procedures group (which comprises the vast majority of the non-elective group; 66.1%). Firstly, the following risk factors showed a significant association with overall AR morbidity (the development of one or more AR morbidities): duration of the anaesthesia, season of the year, periods of apnoea (during induction and/or recovery), hypothermia and a turbulent recovery. Secondly, the following risk factors showed a significant association with AR mild trauma: duration of the anaesthesia, season of the year and a turbulent recovery. Finally, body weight of the patient, body position, duration of the anaesthesia, periods of apnoea (during induction and/or recovery) and problems regarding the intubation are risk factors significantly associated with AR myopathy.

The data suggests a decrease in AR mortality over the past 6 years, compared to both previous data from this clinic and to internationally reported percentages. While AR morbidity may seem to be relatively high, this is likely due to the different definitions used for some morbidities (especially AR mild trauma) and in this light may actually be lower than the rates previously published by other studies. Further research to refine risk factors (e.g. body condition score instead of body weight) is important so that the AR mortality and morbidity risks can be reduced even further over the coming years. When examining the body condition score (BCS) specifically, the current study unfortunately did not gather enough cases with a valid BCS to obtain a reliable outcome on whether it influences the AR mortality and morbidity, and to what extent. Furthermore, increasing the study population would improve the number of significant predictors and the fit of the models. This can be accomplished by collaboration with other (similar) clinics or by expanding the research period. However, the latter makes the analyses of the difference over time more difficult to determine. Most importantly, universally accepted definitions of complications and uniform methods to establish outcome need to be drawn up in order for future studies to be less heterogeneous and more directly comparable.

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