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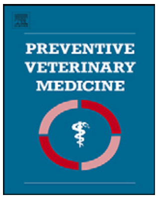

Individual risk factors for Post-weaning Multisystemic Wasting Syndrome (PMWS) in pigs: A hierarchical Bayesian survival analysis

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ABSTRACT

Risk factors for Post-weaning Multisystemic Wasting Syndrome (PMWS) at the pig level were identified using data from a longitudinal study in seven PMWS-affected farms in France. In each farm, a representative sample of 120 pigs (180 in one farm) was randomly selected after farrowing and followed from birth to slaughter. Individual information included serological status for Porcine Circovirus type 2 (PCV-2), Porcine Reproductive and Respiratory Syndrome (PRRS) virus, and Porcine Parvovirus (PPV), individual weight, rearing conditions, and clinical observations recorded at 7, 13, 16 and 21 weeks of age and at slaughter. Two different Bayesian frailty models were used to identify variables related to time-to-PMWS: (i) a logistic-survival model and (ii) an accelerated failure time model (different survival time distributions) both with two levels of clustering (litter and farm). Similar results in terms of variables related to time-to-PMWS were obtained with both models. However, information provided by the different approaches were complementary. Piglets were more likely to exhibit PMWS after early infection by PCV-2 (i.e. before 7 weeks old) and if they were weaned early (before 21 days). Piglets born to PCV-2 seronegative sows and/or to sows with neck injuries due to poorly performed injections were also more at risk. With the accelerated failure time model, time ratios were obtained giving an estimation of the expected survival time (increased or decreased) after exposure to the factor. The logistic-survival model showed that the majority of the risk factors were mostly related to the odds of PMWS whereas the PCV-2 passive immunity derived from the dam also tended to postpone PMWS appearance later.

1. Introduction

Post-weaning Multisystemic Wasting Syndrome (PMWS) has now been observed for more than 10 years after first being described in Canada in 1996 (Clark, 1996; Harding, 1996). Shortly thereafter similar problems were recognized in other countries especially the USA (Kuipel et al., 1998) and in Europe as attested by reports from Spain (Segales et al., 1997), France (Le Cann et al., 1997) and the UK (Allan et al., 1998). The disease was also reported elsewhere in the world, i.e. Eastern Europe (Pejsak et al., 2001) and Asia (Choi et al., 2000). The majority of pig-producing countries were rapidly concerned with the disease which, because of the increased mortality and growth retardation, had huge economic impact on local pig industries. Since late 2004, the eastern part of Canada (province of Quebec) has experienced a sudden re-emergence of the syndrome with a very high level of mortality (Gagnon et al., 2007). The PCV-2 strain in question was called PCV-2b and is apparently closely related to the strains involved in Europe in the late 1990s. Different PCV-2 genotypes have been distinguished (Opriessnig et al., 2006; Grau-Roma et al., 2008) but the relationship between virulence and genotype is still

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debated (de Boisseson et al., 2004; Opriessnig et al., 2006). Although the role of this virus in the syndrome is reinforced by the reported high efficacy of the available commercial PCV-2 vaccines (Kixmoller et al., 2008), the transmission, epidemiology, and factors triggering clinical expression of PMWS are poorly understood.

Although Porcine Circovirus type 2 (PCV-2), a small non-enveloped virus (17 nm) with a single-stranded circular DNA genome was identified as the necessary cause of this syndrome (Meehan et al., 1998), the widespread distribution of this virus for several decades was also demonstrated (Magar et al., 2000; Rodriguez-Arrioja et al., 2000, 2003). Several epidemiological studies carried out in different countries have provided clear evidence of the multifactorial component of the syndrome (Rose et al., 2003; Lopez-Soria et al., 2005; Enøe et al., 2006; Woodbine et al., 2006). PCV-2 is recognized as a necessary associated cause of PMWS together with co-factors of infectious nature (PRRSv, Parvovirus, Mycoplasma, etc.) or co-factors more related to husbandry practices (cross-fostering, mixing in post-weaning facilities, hygiene, etc.). Risk factors were often identified at the farm level and were indicators of the probability that a farm would experience increased mortality due to PMWS. However, only a proportion of the growing pigs within an affected farm actually experienced PMWS (i.e. wasting with typical lesions of lymphoid depletion and lympho-histiocytic infiltrations of various organs). In France, in severe situations, up to 25% of the pigs could be affected by the clinical disease, the remaining 75% being eligible for commercialization. This suggests that within a PMWS-affected farm the likelihood of individual pigs being affected is unequal because of different individual exposures to risk factors. In a previous study preliminary results were obtained for individual risk factors affecting PMWS occurrence (Rose et al., 2005). However, the main aim of this study was to test the effect of the paternal breed on PMWS in the offspring and to test whether the Pietrain breed provided resistance to PMWS after adjusting for different confounding factors (dynamics of PCV-2 infection, PCV-2 status of the dam, rearing conditions).

Longitudinal studies can provide useful information on the circumstances related to the occurrence of a syndrome within a population. Survival analysis is a powerful tool for analyzing such data within a cohort of animals because it identifies variables related to time-to-event occurrence (onset of the disease or death). However the structure of the pig population is rather complex as animals are clustered within litters, within batches and within farms. Thus the study population in such observational surveys is not homogeneous but must be considered as a heterogeneous sample, i.e. a mixture of individuals subjected to different hazards. The non-independence between individuals in a given group can be addressed with frailty models, the "frailty" being the unobserved random proportionality factor that modifies the hazard function of an individual, or of related individuals (Dohoo et al., 2003). In the classical frequentist approach, the available statistical packages usually take only one level of clustering into account. Bayesian methods have been shown to provide flexible and powerful tools for the analysis of complex hierarchical models with several levels of clustering (Hanson et al., 2003; Sanchez et al., 2005; Thurmond et al., 2005; Wintrebert et al., 2005).

The aim of this work was to use the Bayesian approach to analyze survival data from a sample of 900 individual pigs from seven PMWS-affected farms. Cluster effects due to the hierarchical structure of the data (pigs within litters and within farms), were taken into account using frailty models with two levels of clustering. Two approaches were used and compared: (i) the first one was a hierarchical Bayesian logistic-survival model (Hanson et al., 2003), (ii) the second was a Bayesian parametric shared frailty model with different assumptions for the distribution of survival times (log-normal, Weibull and gamma distributions were tested).

2. Materials and methods

2.1. Study design and collected information

A longitudinal study was carried out in seven farrow-to-finish farms affected by the clinical disease during 2004–2005 in France. The seven farms were located in Brittany (western France) and were selected for their severe PMWS status. They were also selected for convenience as the farmer had to agree to the intervention. Diagnosis at the farm level was based on the diagnostic criteria for PMWS in affected pigs as defined by the EU consortium on PCV-2 (http://www.pcvd.org) (Allan, 2007) which include (i) clinical appearance in the herd and a significant increase in mortality due to PMWS and (ii) laboratory examination of necropsied pigs suffering from wasting with evidence of typical histopathological lesions and detection of PCV-2 within the lesions.

After farrowing, all piglets were identified (ear tag) in each batch under study. A representative sample of 120 piglets (180 in farm D because farm C experienced an unexpected low percentage of PMWS pigs) was randomly selected within each farm (proc PLAN (SAS Institute Inc., 2002)) stratifying on the litter (at least 2 piglets per litter). The required sample size was estimated according to the formula described in Schoenfeld and Richter (1982) and based on preliminary results from Rose et al. (2005). Calculations were based on the variable 'PCV-2 status of the dam' because from those previous results only 5% of the pigs were expected to be born to a seronegative dam (highly unbalanced distribution). With an expected HR = 2.3, taking 0.05 for type I error and a power of 0.90, and based on the previously observed median survival time for piglets born to seropositive dams (143 days), more than 820 pigs were estimated to be necessary which leads to 120 piglets per farm. The 900 piglets were individually re-identified at weaning (change of ear tag and tattoo) and monitored until slaughter by clinical observations and individual weighing (at 7, 13, 16 and 21 weeks of age). Clinical observations were performed throughout the study by three specially trained operators. Blood samples were taken at weaning and at 7, 13, 16 and 21 weeks of age. A new needle was used for each pig. The husbandry conditions to which the monitored pigs were subjected (pen area, pig density, hygiene, etc.) were also