Case report: Analysis of risk factors and production effects following an outbreak of bovine respiratory disease in stocker cattle

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Abstract

Risk factors and production losses are reported for an outbreak of bovine respiratory disease (BRD) in stocker cattle in a southeastern US grass-based system. Beef calves purchased from livestock auctions arrived in 2 groups 1 week apart (n=133 and 77, respectively). Cattle were mass-medicated with antibiotics and vaccinated 3 days after arrival, then commingled on ryegrass pasture. A daily BRD score (0-4) based on presence and severity of clinical signs was used to determine antibiotic treatment eligibility over the 150-day stocker phase. BRD morbidity and mortality were 61.9% and 12.9%, respectively. Cattle in arrival group 2 had a greater incidence density of BRD (rate ratio = 1.54, 95% CI: 1.07, 2.22). Odds for death were 5.0 times greater for cattle in arrival group 2 (95% CI: 2.0, 12.2) and 42.5 times greater for cattle diagnosed with BRD (95% CI: 2.5, 713.2). The gain of average daily gain was decreased 0.15 lb/day (0.07 kg/day) in cattle with BRD. Including death loss, calves with BRD gained an average of 64.1 lb (29.1 kg) less than unaffected calves over the stocker phase. Despite metaphylaxis and prompt identification of sick cattle, this BRD outbreak resulted in high morbidity, mortality, and production loss in a stocker cattle system.

Key words: BRD, stocker cattle, outbreak investigation

Introduction

Bovine respiratory disease (BRD) is a multi-factorial disease complex that results in important losses due to morbidity and mortality in cattle at all stages of production.5,8 Cattle in the stocker phase are at risk for BRD due to stressors such as transportation, commingling, and waning maternal immunity.13 Predisposing risk factors for BRD include procurement from an auction market rather than a ranch source, extended shipping times, weather, and age/size of the calf.14 Other stressful procedures at arrival, such as castration and dehorning, have been associated with increased risk for BRD in stocker cattle.314

Bovine respiratory disease is a syndrome rather than an etiologically specific disease; therefore, diagnosis is primarily made by nonspecific clinical signs including ocular or nasal discharge, labored breathing with or without an audible cough, fever, depression, and decreased appetite.7 Severe
Animals

bronchopneumonia may result in death, and pronounced lung lesions are often present at necropsy. Diagnosis by both clinical illness and pulmonary lesions at necropsy results in substantial misclassification of BRD in feedlot and stocker cattle, which may result in underestimation of disease due to poor sensitivity or overestimation of disease from imperfect specificity. Cattle have reduced growth performance during recovery as well as direct death loss, making BRD both animal welfare and production efficiency concerns in stocker operations.

Although BRD can occur sporadically, it more often occurs as an outbreak in stocker and feedlot production systems, typically with the peak incidence occurring 14 days after arrival. Nationally, 16.2% of feedlot cattle developed BRD, and in 1 large feedlot study, annual morbidity varied between 5 and 44% over a 15-year period. Commingling of cattle from multiple sources may play an essential role in the transfer of viral or bacterial agents that contribute to disease. Often, commingling occurs concurrently with additional stressors such as weaning and transportation that may further increase the risk for severe disease or death because of effects that suppress immunity or induce systemic inflammatory responses. Outbreaks of BRD are also frequent in cattle in stocker systems, which contain many of the same risk factors associated with BRD in feedlot cattle including commingling, transportation, and weaning stress. However, there is limited research on BRD in cattle in this segment of the beef industry.

Outbreak investigations can be valuable for understanding and quantifying disease occurrence, identifying risk factors, and formulating preventive measures. This systematic process of data collection and analysis, often combined with onsite evaluation, can provide meaningful insights into the disease process. The objective of this study was to investigate an outbreak of BRD in high-risk stocker cattle to determine risk factors for morbidity and mortality in this segment of the cattle industry, as well as to quantify the effects of the disease on cattle growth performance.

Materials and Methods

Animals

This report describes an outbreak of BRD in stocker cattle after arrival onto rye grass pasture. Male stocker calves were purchased in 2 groups by an order-buyer from multiple auction markets, arriving 38 and 31 days prior to enrollment in a planned parasite study (n=133 and 77, respectively). Arrival weights for cattle were similar for arrival group 1, with a mean weight of 544 lb (247 kg) and a standard deviation of 47 lb (21 kg), and group 2, with a mean weight of 541 lb (246 kg) and a standard deviation of 39 lb (18 kg). Cattle in both groups were processed 3 days after arrival including metaphylaxis with gamithromycin (2 mL/110 lb [6 mg/kg], SQ), multivalent vaccination (IBR, BVD types 1 and 2, PI-3, BRSV, a multivalent Clostridium spp bacterin-toxoid including tetanus, and Mannheimia haemolytica toxoid), surgical scalpel castration of bulls (n=13), and placement of visual and electronic identification (EID) ear tags. Pooled ear notch testing for bovine viral diarrhea virus did not identify any persistently infected cattle.

Cattle groups were commingled and kept on a 25-acre background pasture for approximately 4 weeks, then vaccines were re-administered. Cattle were enrolled in a parasite study (day 0) and stratified by weight and fecal egg count into 1 of 3 treatment groups (injectable doramectin, injectable eprinomectin, or injectable eprinomectin with 10% of cattle left untreated as refugia). Cattle were rotated daily by group among 3 pastures, each divided into 3 sub-pastures. Weights and rectal fecal samples were collected every 4 weeks on all animals through day 112.

BRD diagnosis and treatment

Experienced pen riders performed daily animal observations from arrival until study end. Cattle with suspected illness were removed from the pasture for examination. Trained personnel scored cattle for BRD on a scale of 0-4 based on clinical signs of respiratory disease, where 0 was a clinically normal animal, 1 to 3 indicated mild, moderate, and severe signs of BRD, respectively, and 4 was a moribund animal. Clinical criteria for BRD clinical scoring, modified from Step et al, are reported in Table 1. A diagnosis of BRD was made if assigned BRD score was greater than 0. Treatment was administered if cattle had a BRD clinical score of 1 or 2 in conjunction with a rectal temperature ≥104°F (40°C), or if cattle had a BRD score of 3 or 4 regardless of rectal temperature. Cattle with BRD clinical scores of 4 were treated or humanely euthanized at the discretion of the attending veterinarian depending on severity of disease, prognosis, and assessment of animal welfare.

Cattle with a diagnosis of BRD were eligible for treatment after a 6-day post-metaphylaxis interval had elapsed. At first diagnosis of BRD, cattle received 4.5 mg/lb enrofloxacin (10 mg/kg, SQ) according to label directions. Cattle eligible for a second treatment following a 3-day post-treatment interval were given 3 mg/lb ceftiofur (6.6 mg/kg, SQ) according to label directions. Cattle eligible for a third treatment following a 7-day post-treatment interval were given 9 mg/lb oxytetracycline (20 mg/kg, SQ) according to label directions. All injections were administered in accordance with Beef Quality Assurance (BQA) guidelines.

If cattle met the treatment criteria for BRD in the 3 days after arrival but before processing, gamithromycin was given as a treatment at that time rather than at processing. Animals receiving gamithromycin as metaphylaxis at processing were not counted as treated. All pulls were recorded, including date, reason for pull, BRD score if applicable, any treatment given, personnel, and post-treatment interval. Cattle that died after showing neurological signs and those without any antemortem signs of illness prior to death were submitted for laboratory necropsy at the Mississippi State...
Table 1. Rubric used to assign individual animal daily BRD score based on presence and severity of clinical signs of respiratory disease.

<table>
<thead>
<tr>
<th>BRD score/severity</th>
<th>Clinical criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - None</td>
<td>Clinically normal</td>
</tr>
</tbody>
</table>
| 1 - Mild           | One or more of the following:  
                     - Elevated respiratory rate for the environmental conditions  
                     - Nasal discharge: clear, cloudy, white, or yellow  
                     - Mild to moderate gauntness |
| 2 - Moderate       | One or more of the following:  
                     - Mild or moderate depression  
                     - Lethargic, but may look alert when approached  
                     - Head carriage lower than normal, but may return to normal when approached  
                     - Hiding behavior  
                     - Mild to moderate muscle weakness  
                     - Mild incoordination and/or  
                     - Cross stepping and/or  
                     - Floppy ear carriage  
                     - Moderate to extreme gauntness  
                     - Breathing with mild to moderately increased abdominal effort  
                     - Cattle with a score of 2 may also have elevated respiratory rate for environmental conditions, and/or nasal discharge. |
| 3 - Severe         | One or more of the following:  
                     - Severe depression  
                     - Lethargic and does not look alert when approached  
                     - Low head carriage, does not return to normal when approached  
                     - Does not move away from examiner as fast or as far as expected when closely approached  
                     - Severe dyspnea  
                     - Open-mouth breathing  
                     - Moderately to markedly increased abdominal effort  
                     - Cattle with a score of 3 may also have elevated respiratory rate, nasal discharge, and/or moderate to extreme gauntness. |
| 4 - Moribund       | One or more of the following:  
                     - Recumbent and does not rise when approached or directly stimulated  
                     - Standing but does not move unless directly stimulated  
                     - If the animal moves, if is very weak: drags feet, sways, stumbles  
                     - Eyes may be very sunken, abdomen may be very gaunt  
                     - Moribund animals may also have signs described for score of 1, 2, or 3. |

University College of Veterinary Medicine. Field necropsy was performed on the remainder of dead cattle by 1 of the veterinary researchers or an affiliated university veterinarian. Diagnostic samples were not routinely collected if cause of death was apparent from gross inspection.

Data analysis

The cumulative incidence of BRD was calculated as the number of new BRD cases divided by animals at risk at arrival and the beginning of each subsequent week. Incidence density was calculated as new BRD cases divided by calf days at risk. Days at risk was the sum of the total number of days between arrival and 1) development of BRD for each calf, 2) death, or 3) the end of the 150-day backgrounding period. Factors were tested for association with BRD incidence density using a generalized linear mixed model with a Poisson distribution, and log link and an offset of log of days at risk for BRD (PROC GLIMMIX). Variables tested were arrival group, arrival weight, whether calves were castrated at processing or had been castrated prior to purchase, and fecal egg count measured approximately 30 days after arrival. The model was built using manual forward selection based on Type 3 P-values and model fit. Results were reported as relative risk.

Risk factors for mortality from all causes were analyzed using multiple logistic regression. Manual forward selection was used to develop the final reported model. Because all animals which died during the study had BRD confirmed by necropsy, Firth’s modification for maximum likelihood estimation was used to account for the zero value cell in the contingency table of death by BRD diagnosis (PROC LOGISTIC). Results were reported as odds ratios for an outcome of death.
Of the 130 cattle which developed BRD, risk factors for mortality due to BRD were analyzed as time to event using a Cox proportional hazards model and reported as hazards ratios. Observations were truncated to include only cattle diagnosed with BRD, with survival time measured from the time of diagnosis to death or right censoring at 6 weeks post-diagnosis of BRD to meet the requirement for proportional hazards. Risk factors included in the final model were verified as meeting proportional hazards requirements by graphical and goodness-of-fit tests. Only 2 cattle had a BRD clinical score of 4, so these animals were grouped with BRD score=3. Four cattle first diagnosed with BRD on necropsy were not included in the proportional hazards analysis since they did not show ante-mortem clinical signs of BRD.

The effect of BRD on performance was tested using generalized linear mixed models (PROC MIXED) for the outcomes of average daily gain (ADG) and weight gain. Average daily gain was only calculated for animals surviving to the end of the 150-day observation period, representing a deads-out analysis. Weight gain was calculated for all animals, with those that died during the stocker period having an end weight of 0 lb, and thus represents a deads-in analysis accounting for the effect of mortality on cattle performance. Random effects of arrival group and parasite treatment group to account for clustering effects were used in all linear regression models.

For all analyses, statistical significance was set at alpha = 0.05.

Results

BRD occurrence and incidence

BRD was identified in 130 of 210 calves (61.9%) and, of these, 27 (12.9%) died due to BRD, a case fatality of 20.8% (27/130). Morbidity, mortality, and case fatality by arrival group are shown in Table 2. Figure 1 shows the number of BRD cases and deaths in each arrival group by study day. The weekly cumulative incidence of BRD was highest for both groups 2 to 3 weeks after arrival, followed by a decrease weekly cumulative incidence of BRD was highest for both groups 2 to 3 weeks after arrival, followed by a decrease in weekly incidence with the last case of BRD diagnosed approximately 9 weeks post-arrival (Figure 2). The BRD cumulative incidence for arrival group 2 (53/77=68.8%) and arrival group 1 (77/133=57.9%) were not significantly different (Relative Risk=1.2, 95% CI: 0.8, 1.7). However, incidence density was 1.5 times greater (95% CI: 1.1, 2.2) for arrival group 2 (53/4318=1.2 cases/100 days at risk) compared to arrival group 1 (77/9674=0.8 cases/100 days at risk).

Cattle were treated for BRD 1.7 times on average (101 cattle treated 172 times). Treatment outcomes for BRD cases are summarized in Table 3. Of all treatments given during the study, 85.6% (172 of 201) were for BRD. In addition to BRD, cattle received treatments for several other conditions as per study protocol. Two cattle pulled for lameness were treated with flunixin meglumine1 for soft-tissue injury, with 1 calf receiving additional treatment with florfenicol10 for suspect joint infection. Fourteen cattle were treated with florfenicol for foot rot (2 animals treated twice). Three cattle were treated with oxytetracycline1 for pink eye. Two cattle were treated with flunixin meglumine and ceftiofur1 for marked scrotal inflammation associated with castration, and 2 cattle were treated for neurological disease (1 treated twice and the other 3 times) as described below.

Neurological abnormalities

Four cattle displayed abnormal neurological signs during the study that were severe enough to justify euthanasia. Signs included severe depression, severe ataxia, recumbency, and apparent visual deficits. Two of the cattle received treatment with intramuscular thiamine and intravenous dexa-methasone prior to euthanasia, whereas the other 2 calves had severe, acute disease and were euthanized without treatment. Complete necropsies were performed by pathologists at the Mississippi State University College of Veterinary Medicine. No gross or histopathologic findings were identified that supported a specific diagnosis of the cause of the neurologic signs. All 4 cattle had grossly evident pneumonia.

Risk factors for morbidity, mortality, and mortality due to BRD

BRD incidence density was not associated with arrival weight or whether cattle were castrated at processing. However, fecal egg count measured approximately 1 month after arrival was positively associated with BRD incidence density (RR = 1.04 for every 100 additional eggs per gram, 95% CI 1.01 to 1.07, P=0.006).

The final multivariable logistic regression model for mortality from all causes included 2 risk factors: arrival group and BRD. The odds for death was 5.0 times greater for cattle arriving in group 2 (95% CI 2.0 to 12.2, P<0.001) and 42.5 times greater for cattle diagnosed with BRD (95% CI 2.5 to 713.2, P=0.009).

Table 2. BRD morbidity and mortality by arrival group.

<table>
<thead>
<tr>
<th>No. of cattle</th>
<th>BRD cases (% morbidity)</th>
<th>BRD deaths (% mortality)</th>
<th>Case fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrival group 1</td>
<td>133</td>
<td>77 (57.9)</td>
<td>8 (6.0)</td>
</tr>
<tr>
<td>Arrival group 2</td>
<td>77</td>
<td>53 (68.8)</td>
<td>19 (24.7)</td>
</tr>
<tr>
<td>Overall</td>
<td>210</td>
<td>130 (61.9)</td>
<td>27 (12.9)</td>
</tr>
</tbody>
</table>

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Table 3. Treatment numbers and outcomes for the 130 cattle diagnosed with BRD antemortem or postmortem.

<table>
<thead>
<tr>
<th>No. BRD treatments</th>
<th>No. cattle</th>
<th>No. BRD deaths</th>
<th>Case fatality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>29</td>
<td>4</td>
<td>13.8%</td>
</tr>
<tr>
<td>1</td>
<td>57</td>
<td>9</td>
<td>15.8%</td>
</tr>
<tr>
<td>2</td>
<td>20</td>
<td>8</td>
<td>40.0%</td>
</tr>
<tr>
<td>3</td>
<td>21</td>
<td>6</td>
<td>28.6%</td>
</tr>
<tr>
<td>*4</td>
<td>3</td>
<td>0</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*The BRD protocol included treatment with up to 3 consecutive antibiotics. Cattle which showed clinical signs of BRD in the first 3 days after arrival prior to metaphylaxis were given gamithromycin at the time of diagnosis and were recorded as treated. If eligible for all subsequent treatments, a total of 4 treatments were possible. Apparently healthy cattle receiving gamithromycin at processing were not considered treated.

Multivariable survival analysis identified 2 factors associated with death among cattle with BRD: arrival group and BRD score. The hazard ratio for death was 3.3 times greater for cattle in arrival group 2 (95% CI 1.3 to 8.3, P=0.01) compared to arrival group 1. Cattle with severe respiratory disease (BRD score of 3 or 4) had a hazard 27.1 times greater (95% CI: 1.48 to 496.36, P=0.03) than cattle with a score of 1. However, cattle with a BRD score of 2 did not have significantly greater hazard (Hazard ratio = 5.7, 95% CI: 0.30-109.84, P=0.25) than cattle with a score of 1 (Figure 3).

Cattle performance

Of the 210 stocker cattle initially purchased, 28 died during the study period (27 due to BRD and 1 due to sepsis from a hepatic abscess with concurrent evidence of chronic BRD), and 9 were surplus animals not enrolled in the parasite clinical trial and subsequently were not weighed at the end of the study. End weights were therefore available for 173 cattle and used to calculate ADG. Cattle with BRD and surviving to the end of the 150-day stocker period gained 0.15 lb/day (0.07 kg/day) less than cattle without BRD (95% CI 0.02 to 0.28, P=0.03). Cattle treated for BRD multiple times had lower performance, with ADG decreasing by 0.18 lb/day (0.08 kg/day) for each treatment (95% CI 0.08 to 0.29, P<0.001). Additionally, severity of BRD was associated with cattle performance. Average daily gain was not significantly different in cattle with a maximum BRD score of 1 (P=0.89) compared to cattle never diagnosed with BRD. However, ADG was decreased by 0.14 lb/day (0.06 kg/day) in cattle with BRD scores of 2 (95% CI 0.0 to 0.29, P=0.05) and 0.53 lb/day (0.24 kg/day) in cattle with BRD scores of 3 or 4 (95% CI 0.28 to 0.79, P<0.001) compared to cattle without BRD (Figure 4).

Total gain (end weight - initial weight) was calculated for the 173 cattle surviving until study end and the 28 cattle which died during the study (end weight 0 lb) as a deads-in analysis. Including death loss, cattle with BRD gained 64.1 lb (29.1 kg) less on average than cattle without BRD (95% CI 21.7 to 106.5, P=0.003).
Discussion

This study characterizes a severe outbreak of BRD in high-risk stocker cattle in a grass-based management system typical of southeastern US production systems. The incidence of disease was greatest during the second and third week following arrival, followed by a rapid decline in incidence. Cattle with BRD were more likely to die if they had severe clinical disease as classified by higher BRD scores or were in arrival group 2. Both ADG and weight gain were lower in cattle treated for BRD than those without BRD, indicating that disease negatively affected production during the 150-day stocker phase described in this study.

The cumulative incidence of BRD morbidity in this outbreak was consistent with previous reports describing stocker calves, although the rate of mortality was substantially higher. Of note, high mortality occurred despite the use of gamithromycin as metaphylaxis, an antibiotic recently identified as a top-tier antibiotic for the control of BRD in beef cattle. The higher risk (both incidence density and hazard) for BRD in the second group of cattle to arrive may have been due to cattle developing BRD more quickly, possibly due to being introduced into the midst of an active outbreak, and thus contributing fewer days at-risk to the calculation of incidence density. We speculate that the increased risk of mortality seen in cattle arriving in the second group may have been due to exposure to a higher pathogen load resulting from amplification of respiratory viruses and/or bacteria in the ongoing outbreak involving cattle in the first group. Unfortunately, we cannot be certain of the reason for the greater risk for BRD or mortality in group 2 because the observational nature of this study limits our ability to differentiate this risk factor from other differences between the 2 arrival groups including source, transportation, or auction market commingling.

It was noteworthy that 4 cattle showed abnormal neurological signs of significant severity to warrant euthanasia of 2 cattle, and that ended in death of 2 cattle. No specific cause of the neurological signs could be identified by complete necropsy. Because *Histophilus somni* was isolated from lung tissue of several study cattle with BRD, the abnormal neurological signs may have been due to thromboembolic meningoencephalitis (TEME), although histopathologic lesions consistent with TEME were not identified at post-mortem. Other differentials include polioencephalomalacia, or metabolic abnormalities such as hypocromesemia or acidosis. However, pathologic changes consistent with polioencephalomalacia or acidosis were not seen, and clinical signs were not typical of hypomagnesemia.

Parasitism, as measured by fecal egg count approximately 30 days after arrival, was linearly associated with risk for BRD, with cattle at slightly increased risk for each additional 100 parasite eggs per gram of feces. However, it is unclear if high parasite loads predisposed cattle to BRD or if cattle with BRD were more susceptible to intestinal parasites. Griffin et al reported an increased risk for BRD in cattle with high fecal egg counts at arrival to a stocker operation; however, the temporal relationship between this association was not established in the present study. Other risk factors for BRD morbidity were not identified in this study, but many of the previously reported predisposing factors such as shipping times, animal source, and sex differences between heifers and male calves were not measured. Castration at processing was not associated with greater risk for BRD, but there was very low power to detect a difference with only 13 bull calves processed.

Of the cattle showing clinical signs of BRD, a higher maximum BRD score greatly increased odds for death, indicating that the BRD scoring system as used in this study is a useful approximation of clinical disease severity when scored by experienced observers. For each incremental increase in
BRD score, the hazard ratio increased and survival decreased despite aggressive identification and treatment of clinically ill animals. A guarded prognosis is therefore warranted when cattle have severe clinical disease.

Concurrently, it is important to recognize the limitations of clinical signs as a diagnostic test for BRD which may result in misclassification due to imperfect sensitivity and specificity. White and Renter estimated modest sensitivity for both clinical signs of BRD and lung lesions at harvest, and a prospective longitudinal study by Wittum et al found that only 35% of cattle were treated for respiratory disease while 72% had pulmonary lesions at slaughter. Lung lesions at harvest were not available for cattle in this study, but all 4 of the cattle that were euthanized without clinical signs of BRD had pneumonia at necropsy. The reported incidence of BRD in this study may therefore underestimate the true extent of the disease outbreak.

Diagnosis of BRD negatively affected cattle performance with lower ADG and decreased total gain in cattle. As in previous studies, ADG was decreased with each additional treatment for BRD, indicating that animals with poor response to treatment had lower growth performance than those which recovered from disease. More severe BRD, as determined by clinical severity scores, resulted in greater production losses. Measures such as ADG that are only calculated on animals surviving to market underestimate the cost of BRD on cattle production by excluding losses due to death. A deads-in-analysis may more accurately evaluate the true production cost of a BRD outbreak by taking into account the unmarketed weight of calves lost due to death.

Conclusions

Outbreak investigations provide a useful framework to identify risk factors and production effects during or following the occurrence of disease in animal populations. Substantial morbidity, mortality, and production loss occurred in this group of high-risk stocker cattle despite antimicrobial metaphylaxis. Many management factors, including introducing cattle during an active disease outbreak, may increase risk of BRD morbidity or mortality. Finally, BRD clinical scores may be a useful predictor of mortality.

Endnotes

a Zactran®, Boehringer Ingelheim, Duluth, GA
b Vista 5®, Merck Animal Health, Omaha, NE
c Covexin 8®, Merck Animal Health, Omaha, NE
d Presponse® SQ, Boehringer Ingelheim, Duluth, GA
e Dectomax®, Zoetis, Parsippany, NJ
f Longrange®, Boehringer Ingelheim, Duluth, GA
g Baytril® 100, Bayer, Shawnee Mission, KS
h Excede®, Zoetis, Parsippany, NJ
i Noromycin® 300LA, Norbrook Inc., Overland Park, KS
j Microsoft Excel 2013, Microsoft Corporation, Redmond, WA

k SAS for Windows 9.4, SAS Institute, Inc., Cary, NC
l Banamine®, Merck Animal Health, Omaha, NE
m Nuflor®, Merck Animal Health, Omaha, NE

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References

