Dear Editor:

We appreciate you and the reviewers for the very constructive comments and suggestions to improve our manuscript. We have revised the manuscript according to these comments and have marked the changes with red texts. Some valuable information suggested by the reviewers is also added and discussed. The comments are responded point by point as below.

Response to the Editor’s comments:

1. Please provide more detail of how this was an extension of your previous pilot study.

Response: We have added more detailed description to explain this current study an extension of our pilot study in the revised introduction section as well as in the method section (pages 7 and 8). We addressed that despite our pilot study of pediatric patients with various NMDs has demonstrated the feasibility of this combined noninvasive approach, due to the limited patient numbers and relatively shorter time frame of the study, the effectiveness of such treatment is still unclear and the outcome predictors remain unknown. Therefore, we conducted this extensive study to validate its effectiveness and try to identify potential outcome predictors.

2. Efficacy is usually assessed under “ideal” conditions (e.g. via RCT), whereas effectiveness is measured in “real-world” conditions (e.g. via the observational study). If your study assessed efficacy, please elaborate on how the “ideal” conditions were ensured.

Response: Thanks for your comment. As for your suggestion, in the title and revised context, we have correct the term of efficacy to “effectiveness” since our study is not a RCT designed. The description of effectiveness would be more appropriate for the real-world conditions of our observational study.

3. Please ensure that the study reporting adheres fully to the STROBE guidelines.

Response: We have completed STROBE checklist and submitted it as a supplementary file.

4. Regarding a statement on informed consent for the present study is required or waived.

Response: In the present study, the need for consent was waived under the agreement of our IRB. We have specified this issue and provided the reasons for the waiver of informed consents in the revised method section (page 9).

5. Please move the ethics approval and informed consent statements to the methods section, and delete from the declarations page.
Response: As for your instruction, we have moved the ethics approval and informed consent description from the declarations page to the revised method section (pages 8-9).

6. Please confirm in the methods that all treatments were provided according to standard clinical care.

Response: As for your suggestion, we have added the description in the revised method section confirming that all treatments were provided in the present study according to the standard clinical care guideline for NMD patients (page 9).

Response to Reviewer 1’s comments:

1. This study cannot identify the efficacy of NIV and MIE as there is no patients in the control group (without NIV and MIE). It only can identify the associations between outcomes and NIV + MIE. The aim of this study should be revised as well as the introduction section.

Response: As for your suggestion, we admit that our study is not an RCT designed study, therefore, using the term of “efficacy” might be inappropriate. We have amended the description of our study aim in the revised introduction section (page 7). Furthermore, in the title and main context, we have also corrected the term “efficacy” to “effectiveness” to more fit the real-world conditions of our observational study.

2. The current study only finds the predictors of treatment failure. How to use these predictors is more important. In table 3, adding a cutoff value is encouraged. Adding a multivariate analysis also can improve the strength of the evidence.

Response: Thanks for your valuable suggestion. We have added a multivariate analysis and a cutoff value of outcome predictive factors in the revised Table 3 and main context (pages 14 and 20).

3. As this is a PICU, why the range of age is 0.17-39 in total cases?

Response: We admit that there was a wide range of age of enrolled cases in the present study. There are the reasons why we enroll patients with an extensive age range in a study: (1) The most patients whose genetic mutation and muscle histopathology was diagnosed by our pediatrician at their childhood. We provide care for these patients since childhood, and most of them, extending to their adulthood. Therefore, when they encounter ARF episodes even at adulthood, they would prefer PICU admission for consistent care. (2) In our institute, we have set a neuromuscular clinic providing care and consultation for NMD patients including children and adults. The most health care providers of this multidisciplinary team are pediatricians. Therefore, NMD patients admitted to our hospital agree that pediatric ward settings can provide more comprehensive care specified to their underlying NMD. We have added these explanations to the patient information in Method section (page 8).
Nevertheless, we did put age into a variable during analysis, and as shown in Table 2, we found that age did not affect the NIV/MI-E outcome significantly.

4. The youngest patient is 2 month. How to use the machine of noninvasive ventilator?
Response: Thanks for your comment and question. Yes, we apply Respironics®, Murrysville, PA for the 2-month-old infant. As reported by previous studies regarding NIV on the young infant, they suggested that except for the sophisticatedly settings of NIV, the greatest obstacle for applying NIV successfully in infants and young children is the availability of an appropriate interface. Indeed, we used the Respironics® (Murrysville, PA) pediatric nasal mask with comfort flap and small child headgear to reduce the poor cooperation of NIV delivery on the young infant. In the revised Method section, we have also raised this issue and added the description of choosing interface for young infants (pages 10-11).

5. How long the NIV was used every day? How many times of MIE applied every day?
Response: About the duration of NIV use per day, we have added the description of the protocol of NIV delivery in the revised Method section (page 10). We also added the information about subsequent adjustment as “On subsequent days, ventilatory assistance was gradually reduced, depending on the clinical status. (page 11)” As a result, the mean time from onset to minimal NIV settings was 40.2 ± 11.8 min in all patients (page 16). Finally, as in the Table 2 of our original manuscript, we had provided the information regarding the total duration of NIV use between success and failure groups (Row: NIV duration (d)).

About the frequency of MIE use per day, we have listed the protocol of MIE in the Method section (pages 11-12). Furthermore, in the revised Result section, we added the information of MIE frequency applied on enrolled subjects (page 18).

Response to Reviewer 2’s comments:

1. It is essential the authors clearly underline that careful evaluation of deglutition ability should be performed when deciding to adopt the non-invasive approach in NMD patients with ARF and that patients with bulbar muscle compromise should be excluded from this strategy.
Response: We are appreciated for your valuable comments. We also agree that patient’s ability to adequately protect the upper airway is crucial to the success and safety of NIV. As for your suggestion, we have added more descriptions to clearly underline the evaluation of swallowing ability of enrolled NMD patients and how to exclude those with severe bulbar weakness in the revised Method section (page 10). Furthermore, we also addressed the association between swallowing and NIV/MIE effectiveness in the revised Discussion section (pages 24-25).
2. According to the literature on NIV use in the acute setting, these authors could expect that the outcome of patients with hypoxemic RF was less positive compared to those with CO2 retention. This point needs to be effectively addressed...

Response: As for your suggestion, we have added the description as well as associated references in the revised Discussion section (page 23).

Finally, we sincerely hope this revised manuscript will fulfill the quality of your journal. If you still need any other additional information, it is our pleasure to supply it. We are looking forward to hearing a further message from you. Thank you again for your precious assistance.