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ORIGINAL ARTICLE

The Association Between Plasma Natural Antibodies and Inflammatory Biomarkers Two Weeks After Calving in Cows with No Dry Period

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ABSTRACT

Introduction: Improved energy balance, metabolic status, and natural antibodies (NAb) has been shown in cows with no dry period, however these cows showed increased inflammation status in early lactation. The aim of this study was to determine the association between plasma natural antibodies and inflammatory biomarkers in cows with no dry period during the first two weeks postpartum. **Methods:** Holstein-Friesian dairy cows (n=55) were selected. Before enroll to the experiment, cows were clinically healthy. Plasma samples were collected at week 1 and 2 after calving and were analyzed for NAb binding megantura-keyhole limpet hemocyanin and inflammatory biomarkers. **Results:** Cows with no dry period in this study had an improved energy balance and maintain NAb titers but increased ceruloplasmin (inflammatory biomarkers) in early lactation. In this study we found a significant correlation between NAb IgG binding KLH and haptoglobin in plasma ($P<0.01$). However, there were no correlations between albumin, cholesterol and NAb (IgG and IgM) binding KLH. **Conclusion:** This study demonstrate that cows with no dry period have an improved energy balance and maintained the level of natural antibodies in plasma. Moreover, IgG titers in plasma might be correlated with haptoglobin due to inflammation during calving until 2 wk postpartum.

Keywords: Continuous milking, Inflammation, Antibodies

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INTRODUCTION

During transition period, immune status in dairy cows were suppressed and need to be increased. It is known that dairy cows are characterized with immune suppression during transition period, which is related with severe negative energy balance (EB), and high rate of infection diseases and metabolic disorders (8). Innate immunity is the first line defense against infection (1), and natural antibodies (NAb) are a part of humoral innate immunity before get any antigenic stimulation (2). CD5+ B-1 cells produce natural antibodies in healthy individuals and NAb mainly consist of immunoglobulin M (IgM), IgG and IgA (3,4). In previous research, NAb binding keyhole limpet hemocyanin (KLH) were higher in cows with an

improved EB in early lactation (7). Transition period is the crucial time for dairy cows especially in the first two weeks after calving. In early lactation, cows experienced negative EB, which is related to immunosuppression (9). Negative EB was not only related to NAb but also was associated with enhanced level of inflammatory biomarkers (10) and metabolic disorders (11) in dairy cows during early lactation.

In early lactation, increased disease rates are commonly reported among high-yielding dairy cows and characterized by the occurrence of an inflammatory response indicated by acute phase protein (APR) (12). Inflammation evokes white blood cells (WBC) to release of tumor necrosis factor-alpha (TNF- α) and (interleukin-1 and -6) (IL 1 or 6). As a consequence, TNF- α and IL-1 or 6 triggered the release of acute phase response (13). During the response of acute phase protein, positive acute phase reactants (+AP) including haptoglobin and ceruloplasmin were increased in plasma and negative

acute phase reactants (-AP) including cholesterol and albumin were reduced in plasma (13,14).

Cows with no dry period had better energy and metabolic status (15), however these cows had higher ceruloplasmin and oxidative stress compared with cows with a 60-d dry period (10). In an earlier study, cows with no dry period had a higher plasma NAb (IgG) binding liposaccharide (LPS), and higher NAb (IgG and IgM) binding KLH and LPS in milk compared with cows with a short or conventional dry period (16). The relationship between inflammatory biomarkers and NAb titer in plasma during the first two weeks after calving in cows with no dry period are less known. The objective of this study was to determine the association between plasma NAb and inflammatory biomarkers (haptoglobin, ceruloplasmin, albumin and cholesterol) in the first two weeks after calving in cows with no dry period.

MATERIALS AND METHODS

Animals and Experimental Design

All experimental procedures involving animals were approved by the Institutional Animal Care and Use Committee of Wageningen University. The registration number of the experimental protocol was 2010026. The experimental design was described in our earlier study (11). In present study, we investigated data of inflammatory biomarkers and NAb titers from cows with no dry period from earlier study (10). Holstein-Friesian dairy (n=55) were selected from the Dairy Campus research herd. Cows were housed in a freestall with slatted floor and cubicles. Cows were milked twice daily (0500 and 1630 h).

Rations

Ration composition was described earlier (11). Prepartum, cows with no dry period received a lactating cow ration supporting 25 kg of milk yield per day. Forage composition during prepartum and postpartum-treatments consisted of grass silage, corn silage, wheat straw, and a protein source with different ratio. Rations were isocaloric. Concentrate and forage were supplied separately and provided ad libitum.

Blood Sampling

Blood samples were taken from all cows (n=55) in the morning from the tail vein at week 1 and 2 postpartum. Blood samples collected in evacuated tubes containing lithium-heparin and immediately put on ice. All blood samples were centrifuged at 3,000 × g for 15 min at 4°C., frozen, and stored as plasma at -20°C until use.

Laboratory Analysis

Natural antibody titers binding Megathura crenulata-derived KLH (Sigma, H7017 Sigma Aldrich Co., St Louis, MO) in plasma of cows were measured by an indirect enzyme-linked immunosorbent assay (ELISA) technique as outlined in previous study (16). In brief,

titers of natural antibodies in plasma of IgG and IgM isotype were detected using 1:20,000. IgG and IgM were detected using diluted sheep anti-bovine IgG-heavy chain conjugated to horseradish peroxidase (Cat. No. E10-118P, Bethyl Laboratories) and rabbit anti-bovine IgM-whole molecule conjugated to horseradish peroxidase (Cat. No. A10-100P, Bethyl Laboratories), respectively. During ELISA, both IgG and IgM used four-step serial dilutions and started with the ratio 1:40. After washing, a substrate containing tetra methyl benzidine (TMB from Sigma) and 0.05% distilled water was added. The plates were incubated for 10-15 minutes at room temperature and the reaction was stopped by adding 1.25 M sulfuric acid. To measure the extinctions of the titers of IgG and IgM, a Multiskan reader with a wavelength of 450 nm was used.

Inflammatory biomarkers were measured using a clinical auto-analyzer (ILAB 650, Instrumentation Laboratory, Lexington, MA, USA). In current study, the level of total cholesterol, albumin, haptoglobin and ceruloplasmin was determined with the method described and were standardized for each assay (21).

Statistical Analysis

Data were analyzed using the Statistical Analysis System (SAS, version 9.4). To assess associations of NAb (IgG and IgM) titers binding KLH with inflammatory biomarkers (haptoglobin, ceruloplasmin, albumin and cholesterol), the titers from week one and two were added as a linear covariate to developed statistical logistic regression model. The regression coefficient (β) from the statistical model and the p-value corresponding to the β are displayed.

RESULTS

Inflammatory biomarkers and natural antibodies

In the current study, cows with no dry period were investigated for the associations between inflammatory biomarkers and natural antibodies in plasma in the first two weeks postpartum. Earlier study found that cows with no dry period in present study compared with a short or a conventional dry period had higher cholesterol, higher ceruloplasmin and tended to have higher haptoglobin levels in plasma in early lactation (10). The increase of haptoglobin levels in plasma was earlier related with high production of liver macrophages (known as Kupffer cells) during inflammation (22-24). Previous studies showed a positive relationship between plasma ceruloplasmin levels and clinical health problems in cows in early lactation (25-27).

Cows in the current study not only had higher inflammatory biomarkers (haptoglobin and ceruloplasmin) but they also showed increased NAb binding KLH in early lactation (16). Our earlier study showed that the higher NAb binding KLH was associated

with mammary health in early lactation. The levels of inflammatory biomarkers and plasma antibodies binding KLH for cows with no dry period in the first two weeks after calving are shown in Fig 1, 2 and 3.

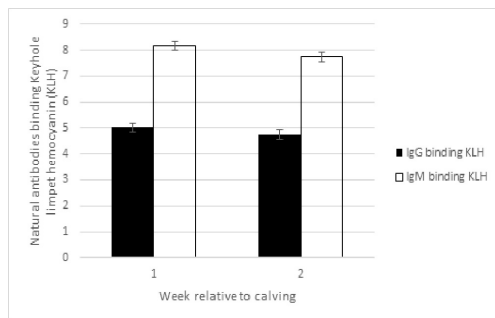


Fig. 1 : Natural antibodies for isotype IgG and IgM binding keyhole limpet hemocyanin in plasma of cows with no dry period in the first two weeks after calving . Values represent means \pm SEM.

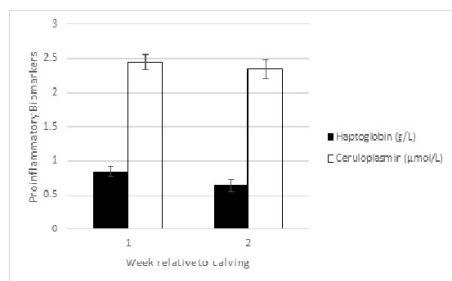


Fig. 2 : Proinflammatory biomarkers for haptoglobin and ceruloplasmin in plasma of cows with no dry period in the first two weeks after calving. Values represent means \pm SEM.

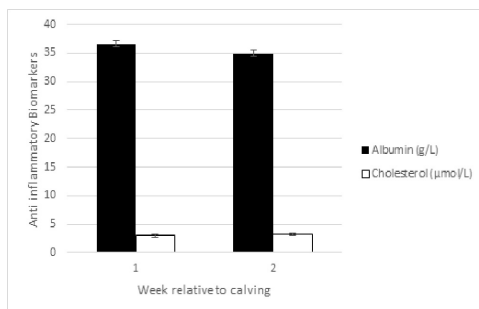


Fig. 3 : Antiinflammatory biomarkers for albumin and cholesterol in plasma of cows with no dry period in the first two weeks after calving. Values represent means \pm SEM.

The association between inflammatory biomarkers and natural antibodies

The association between inflammatory biomarkers and NAb binding KLH in cows with no dry period in the first two weeks postpartum are shown in Table I. In the current study, we found a positive relationship between NAb IgG and haptoglobin levels in plasma ($\beta = 0.97$, $P = 0.03$). The increased plasma NAb IgG binding KLH levels were accompanied by an increased plasma haptoglobin levels. In addition, our study indicated that the increased plasma NAb IgG

binding KLH levels tended to be related with increased ceruloplasmin levels ($\beta = 0.45$, $P = 0.11$), at least in the first two weeks after calving. The positive association between IgG and (+) acute protein response could be related with a severe inflammatory condition (14) of cows with no dry period in early lactation. In the current study, we did not find any association between IgM binding KLH with inflammatory biomarkers.

Table I : Regression coefficient (β) and P -value of plasma natural antibodies (NAb) binding keyhole limpet hemocyanin (KLH) related to haptoglobin, ceruloplasmin, albumin and cholesterol in dairy cows with 0-d dry period in the first two weeks after calving

Variable	IgG binding KLH		IgM binding KLH	
	β	P -value	β	P -value
Haptoglobin (g/L)	0.97	0.03	0.4	0.17
Ceruloplasmin (µmol/L)	0.45	0.11	-0.06	0.74
Albumin (g/L)	-0.01	0.82	-0.03	0.46
Cholesterol (µmol/L)	0.18	0.35	0.03	0.79

DISCUSSION

In the current experiment, cows with no dry period had improved EB and lower daily milk yield with similar dry matter intake (15). In addition, cows with no dry period had higher NAb titers (16) and inflammation status. It was suggested that the higher NAb titers for cows in plasma with no dry period are related with the improved EB (16). In our earlier study, specific plasma NAb were associated with high somatic cell count (SCC) and clinical mastitis. Our earlier study showed that “increasing plasma NAb titer for IgM binding KLH in the week before the occurrence of high SCC were associated with a decreased odd of high SCC occurrence. Moreover, increasing titers of IgM binding KLH or LPS in plasma in the three weeks before the incidence of the disease was associated with decreased odds of CM occurrence” (10 p. 8). It was suggested that NAb levels in plasma or in milk, may be an additional health biomarker to select for mastitis resistance in dairy cows (28,29).

In the current study, high SCC in cows with no dry period was not associated with inflammatory biomarkers (10). There were several causes for inflammation during transition period such as differentiation of mammary gland cell and high oxidative stress (30). A previous study showed that cows with subclinical mastitis (31) and clinical mastitis (32) had increased haptoglobin levels in plasma. Haptoglobin is an acute phase protein synthesized in the liver in response to inflammation (33) and it can be measured in serum. Haptoglobin binds to haemoglobin and so inhibits bacterial proliferation by reducing the availability of iron. Haptoglobin measurement has been of particular interest for detecting

inflammation in cattle and dairy cows due to its virtual absence in the serum of healthy animals (34). Moreover, haptoglobin is more commonly available as a routine analysis compared with many other acute phase protein. Ceruloplasmin is plasma α -2 glycoprotein and one of the important positive acute phase protein. Ceruloplasmin plays an important role for immune system which help to transport copper in the blood by the enzymes lysyl oxidase and Cu-Zn superoxide dismutase. Moreover, ceruloplasmin involved in iron metabolism (ferroxidase) (35). As we know, copper improves immune function by acting on the levels of various enzymes mediating the antioxidant system and protects cells against oxidative damage. Low level of ceruloplasmin in plasma decreased phagocytosis and antimicrobial therefore increase inflammatory conditions (36).

In the previous study, some clinical health problems like fever, metritis, mastitis, retained placenta) were related with high levels of ceruloplasmin and a tendency for high haptoglobin levels in plasma (10). A previous study reported that clinical health problems has been associated with consequences of prolonged inflammations before calving (37). It seems that the increases of inflammatory biomarkers and NAb in plasma were correlated not only due to specific diseases or health problem but may be due to several causes of inflammation conditions in early lactation.

CONCLUSION

In conclusion, a positive correlation between haptoglobin and natural antibodies IgG binding keyhole limpet hemocyanin were found in the first weeks after calving in cows with no dry period. The association between components within immune responses showed complex cause-effect of defensive effect in the body. An inflammatory status and antibody responses attributed to negative EB should be disentangled in various subclinical and clinical health problems related with inflammation may partly explain the changes in inflammatory biomarkers in early lactation.

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ORIGINAL ARTICLE

A Comparative Study Between Filtered Back Projection (FBP) and Sinogram-Affirmed Iterative (SAFIRE) Reconstructions on HRCT Chest of COPD Patients to Measure the Quantity of Emphysema and Lung Volumes

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ABSTRACT

Introduction: *Chest High Resolution Computed Tomography* (HRCT) plays a role in determining the emphysema severity levels of COPD patients by measuring the *low-attenuation volume* (LAV) of the lung parenchyma. **Methods:** This can be used as an alternative to calculate the lung volumes and provide additional information on the pathology that causes both the increase and the decrease of lung volumes. Generally, the reconstruction of raw data in HRCT uses *Filtered Back Projection* (FBP). Nowadays, reconstruction technology that can be used as an alternative for HRCT is reconstruction iterative (IR) to maximize the diagnosis information and the image quality in a low radiation dose. *Sinogram-Affirmed Iterative Reconstruction* (SAFIRE) is an iterative reconstruction using *noise modelling* technique. The research aimed at comparing the use of FBP reconstruction using SAFIRE to measure the quantity emphysema and lung volumes. **Results:** A reconstruction using *window lung filter kernel B70f sharp* and reconstruction using SAFIRE *soft tissue standard I70f sharp* were performed to 40 samples. A post-processing, then, was conducted to each of the reconstruction result to measure the quantity of emphysema by displaying the *Low Attenuation Volume* (LAV%) values and lung volumes (ml). **Conclusion:** The result of the research shows that the use of reconstruction using SAFIRE can affect the measurement result of the quantity of emphysema and lung volumes quantitatively by using a post-processing software when compared to the reconstruction using FBP with the significant values ($p < 0,05$).

Keywords: FBP, SAFIRE, HRCT, Iterative Reconstruction, COPD, Emphysema Quantity, Lung volumes

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a respiratory disease that has become one of the leading causes of death. COPD includes emphysema and chronic bronchitis (1). Based on the previous studies involving 13 Asian countries, the highest prevalence of COPD due to smoking habits is Vietnam, which is 6,7% and the lowest one is Hongkong, which is 3.5% (2). Meanwhile, in Indonesia, the prevalence of COPD is 3,7%. This is closely related to the increase

of smoking habits of people above 15 years old from 34,2% in 2007 to 36,3% (3) in 2013.

As parts of COPD, emphysema can be diagnosed through the CT-Scan examination. *High Resolution Computed Tomography* (HRCT) *Chest* can play a role to determine the emphysema severity levels and the distribution of disease patterns by measuring the *Low-attenuation areas* (LAA) or low-attenuation volume (LAV) on the lung parenchyma (4). HRCT can also be used as an alternative to calculate the lung volumes by using a *post-processing software*, providing additional information in diagnostic pathology towards the causes of either the increasing or decreasing volumes of the lung (5).

The development of the role of the *Computed Tomography*, especially HRCT *Chest* is aligned with the development of technology aiming at maximizing diagnosis information and image qualities with minimum radiation doses. As a result, in the last decades, algorithm iterative reconstruction method has been developed (6). Sinogram-Affirmed Iterative Reconstruction (SAFIRE) is one of the iterative algorithm reconstruction methods that uses noise modelling technique (7). SAFIRE has 5 (five) levels of iterative power equal to the levels of minimizing the noises that have been produced. According to the image quality, level 5 (five) has the lowest value and displays artefacts although the noises produced are minimum. Meanwhile, level 1 (one) has a value close to the FBP reconstruction and gives little effect on the *noise* reduction (8,9). Consequently, it has the potential to be used on SAFIRE level 2,3 and 4.

Before the iterative algorithm reconstruction was developed, *Filtered Back Projection* (FBP) became the reconstruction method used for CT-Scan images (10). Many studies used it as a reference of HRCT Chest to measure the lung volumes and the quantity of emphysema (4,11,8).

This research aims at comparing FBP to SAFIRE in the measurement of the quantity of emphysema and lung volumes

MATERIALS AND METHODS

Samples

Approved by Radiology Department Bach Mai Hospital, this research was retrospective and the data were obtained from Radiology Center of Bach Mai Hospital, Vietnam. We excluded samples that met the following criteria: 1) COPD Patients with ventilators, 2) Cutis emphysema, 3) Chest trauma, 4) Field Of View (FoV) that does not include the entire lung, 5) Beam hardening artefacts in lung parenchyma.

CT Scan Technique

Data were obtained from patients that had undergone HRCT Chest without contrast using modalities of CT-Scan Siemens SOMATOM Definition EDGE 128 Slice retrospectively for 3 (three) months by using parameters including Care kV semi 120 kV which is recommended for the adult patient also will be optimal to combine with Activated Care Dose 4D, recon slice thickness 1.0 mm. The data were, then, collected and reconstructed by using kernel filter B70f sharp lung window and SAFIRE soft tissue standard I70f sharp level 2,3 and 4 shown in Figure 1.

Each result of the reconstruction was processed by using 3D Pulmo software in SYNGO.VIA Siemens workstation to measure the quantity of emphysema by displaying the Low Attenuation Volume (LAV) with HU values of -950 in percentage (%) and lung volumes by showing

the symbol of vol in milliliter (ml) while visually the software allows masking the area with certain HU and calculating automatically from Dicom formatted images of HRCT Chest. The area with <-950HU which is detected as emphysema is shown in blue while the airway showed in red shown in Figure 2.

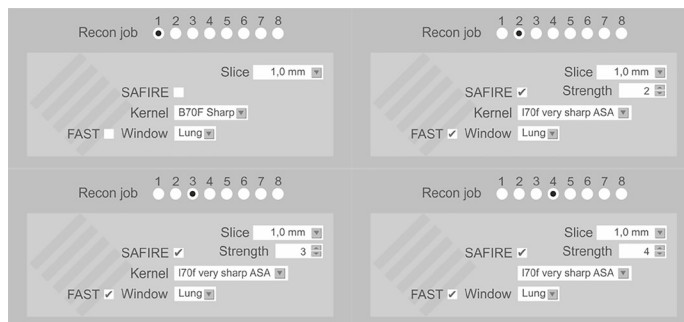


Figure 1 : Parameter Setting in FBP B70F Sharp and SAFIRE I70f (level 2,3,4). The data were, then, collected and reconstructed by using kernel filter B70f sharp lung window and SAFIRE soft tissue standard I70f sharp level 2,3 and 4. Various studies using FBP B70F Sharp as a standard filter in Chest HRCT reconstruction because it can increase spatial resolution which is an important aspect in Chest HRCT.

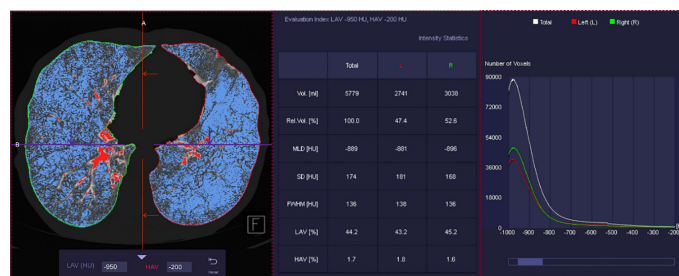


Figure 2 : Measuring the Quantity of Emphysema (LAV%) and Lung volumes. Each result of the reconstruction was processed by using 3D Pulmo software in SYNGO.VIA Siemens workstation to measure the quantity of emphysema by displaying the Low Attenuation Volume (LAV) with HU values of -950 in percentage (%) and lung volumes by showing the symbol of vol in milliliter (ml). The software allows masking the area with certain HU and calculating automatically from Dicom formatted images of HRCT Chest. The area with <-950HU which is detected as emphysema is shown in blue while the airway showed in red.

Statistical Analysis

The normality test used Shapiro-Wilk test. If the data showed normal distribution, it would be analyzed with ANOVA tests. However, if the data did not display normal distribution, it would be analyzed with Wilcoxon test.

The statistical analysis was performed by using SPSS 25.0 (SPSS, Chicago, IL). A p-value of ≤ 0.05 was used to represent the statistical significance.

RESULTS

40 samples, consisting of 39 (97,5%) males and 1 (2,5%) female, were obtained from December 2018 to February 2019. The average age was 65,4 years old (ranging from 36-81).

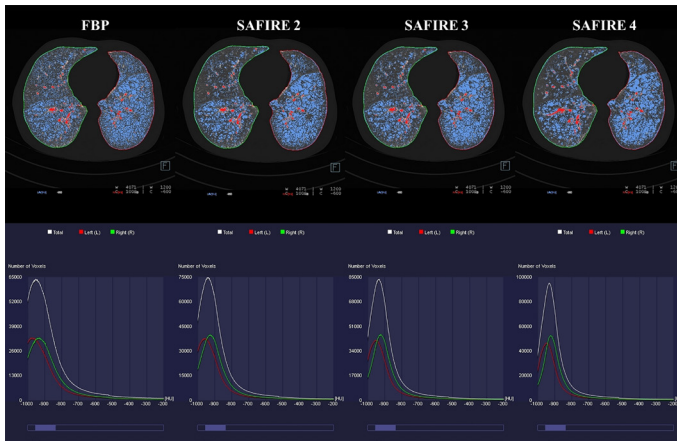
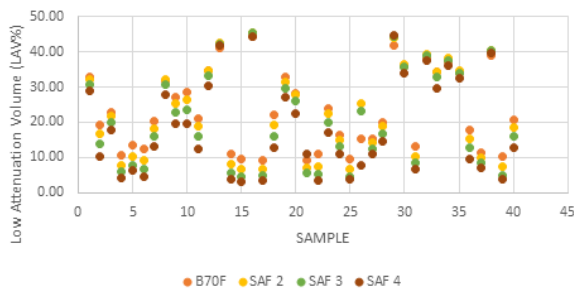
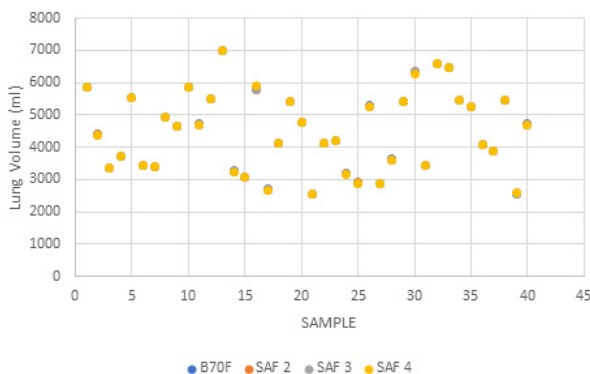


Figure 3 : Shifting in the Histogram of Attenuation Value Distribution. Histogram of attenuation value distribution is one of feature of 3D Pulmo software in SYNGO.VIA that displays a detailed distribution of the Hounsfield Unit (HU) in the voxel of lung area. The implementation of the change of attenuation value distribution can be visually seen from the segmentation result of low attenuation area (LAV) with the threshold of -950HU. There is a shifting of the distribution of attenuation values which move away from the threshold <-950HU, along with the increasing number of the voxel areas in which the distribution of the HU values moving away from the threshold <-950HU

Every reconstruction showed the value distribution of the quantity of emphysema in percentage (LAV%) and lung volumes in millilitre. The distribution of LAV% is shown on Graph 1 and lung volumes is shown on Graph 2.



Graph 1 : Low Attenuation Volume (LAV%) Distribution



Graph 2 : Lung Volume (ml) Distribution

The significance analysis performed by using Wilcoxon test displays a significant difference on the value of the quantity of emphysema (LAV%) between FBP B70F, SAFIRE I70f level 2,3 and 4 ($p < 0.05$). Meanwhile, the significance analysis by using ANOVA showed a significant difference on the value of lung volumes (ml) between FBP B70F, SAFIRE I70f level 2,3 and 4 ($p < 0.05$).

DISCUSSION

The Quantity of Emphysema (LAV%)

There are factor affecting the value of the quantity of emphysema (LAV%), one of which is the algorithm reconstruction that was used in HRCT Chest (12). In this research, the value of LAV% from the use of FBP B70F reconstruction and SAFIRE I70f (level 2, 3,4) showed diverse results and, even, significant differences. The result was supported by the research conducted by Choo et al (13) showing the significant differences in the value of the quantity of emphysema (LAV%) or *emphysema index* (EI) between FBP reconstruction on the two types of IR. Baumuller et al (4) also found the similar result showing significant differences in the value of the quantity of emphysema (LAV%) or emphysema index (EI) between FBP reconstructions on one type of IR consisting of various levels.

The consistence of the result of the research confirming the influence of algorithm reconstruction used to produce the value of the quantity of emphysema is based on the theory carried out by Mets et al's (14) research stating that the use of iterative reconstruction on the basis of noise reduction affects the distribution histogram of the attenuation value of lung parenchyma. Areas with low attenuation that is segmented as emphysema has Hounsfield Unit (HU) values below the optimal threshold, -950HU. The noise reduction using iterative reconstruction has a potential to turn the HU values from below the threshold to be equal or above the threshold so that the values will not be segmented as an area that has low attenuation with emphysema (4). SAFIRE as an iterative reconstruction used in this research focused on the noise modelling aimed at reducing noise. It has 5 (five) levels. The higher the level, the stronger the noise reduction (7). Therefore, every level in SAFIRE change the distribution histogram of different attenuation values.

This research used SAFIRE I70f level 2, 3 and 4. As previously mentioned, SAFIRE levels can make changes on the distribution histogram of the different attenuation values due to different noise reduction. The research shows that SAFIRE I70f level 2 has the least significance on FBP B70F. Meanwhile, SAFIRE I70f level 3 and 4, respectively, has the most significance on FBP B70F.

The implementation of the change of attenuation value distribution can be visually seen from the segmentation result of low attenuation area (LAV) with the threshold

of -950HU shown on Figure 3. The samples illustrates that the value of the quantity of emphysema (LAV%) produced on FBP is 33,00%, while on SAFIRE level 2 is 32,30%; SAFIRE level 3 is 30,70%; and SAFIRE level 4 is 28,90%. This indicates that in the histogram there is a shifting of the distribution of attenuation values which move away from the threshold <-950HU, along with the increasing number of the voxel areas in which the distribution of the HU values moving away from the threshold<-950HU.

According to the result of the statistical test Wilcoxon, there was a change in the significance. Not only did the LAV% values decrease, but the LAV% values in each reconstruction also increased. 10 samples (25%) showed the increase or overestimation, while 30 samples (90%) suggested the decrease or underestimation. The range of decreases and increases varied from -0,10 to +15,50 where the differences were obvious. The result of this research is supported by the one conducted by Choo et al (13) who classified the quantity of emphysema and, then, calculated the LAV% values of the results of FBP and IR reconstructions. The research revealed that both groups of LAV% values or emphysema index (EI) decreased when compared with the LAV% values or emphysema index (EI) in FBP reconstruction.

As previously stated, the SAFIRE treatment is an effort to maintain the image quality by reducing the noise. Research conducted by SYang et al (9) showed that there was a noise value reduction in both FBP B70F and SAFIRE I70f reconstructions. The noise occurred due to a fluctuation of CT Number or Hounsfield Unit on the homogenous tissues or materials (15). In a CT Scan device, if one figure with homogenous materials and CT-Number are found in the area, the CT- Number will have various values around the average or mean values. The theory correlated with an attempt to reduce noise on SAFIRE can minimize the fluctuation of HU values in a homogenous tissue. Therefore, there are two possibilities justifying how the underestimation and overestimation on the LAV% values can occur. First, noise reduction can reduce the fluctuation of HU values in the area with normal HU (without emphysema), so some of the areas become homogenous, leading to low HU values (<-950HU) called overestimation. Second, noise reduction can reduce the fluctuation of HU values in the area with low HU (emphysema), so some of the areas become homogenous, leading to normal HU values (>-950HU) called underestimation.

Referred to Goddard Scale (16), severity levels of emphysema were determined by using the values of the quantity of emphysema. Goddard Scale (GS) provides specific evaluation from the percentage of the emphysema quantity values in three lung zones so that the clinical change of the emphysema quantity values, i.e. underestimation or overestimation, can

affect the representation result for the Goddard Scale to determine the emphysema severity levels which can be classified into mild, moderate, and severe emphysema.

Lung volumes

Besides the value of the quantity of emphysema (LAV%), this research also discusses the significance values of lung volumes in both FBP and SAFIRE I70f (2,3,4) reconstructions. Research performed by Baumueller et al (4) states that the changes in the lung volumes as a result of segmentation is related to the lung density range which indicates the range of HU values in lung parenchyma by combining the entire volume data. The factor is essential as it affects the differentiation between lung parenchyma and extrapulmonary structures, such as soft tissue, bones and airways. Insignificant change in the lung density range will not affect the segmentation process of lung volumes, while the significant one will change the lung volumes.

According to the statistical analysis, the values of lung volumes in every reconstruction are significantly different. The significance deals not only with the decrease of the values of the lung volumes but also with the increase one in every reconstruction. Compared to the FBP B70F reconstruction, the entire samples of the result of SAFIRE I70f reconstruction show an increase or overestimation in 9 samples (22,5%) and a decrease or underestimation in 31 samples (77,5%).

When correlated with the theory in Baumueller et al's research (4), the changes in lung volumes can be caused by the significant change in lung density range that affects the segmentation process. The implementation of lung density change might not be able to be visually seen through the segmentation result, but it can be assessed through the histogram of the attenuation distribution that shows the shifting in HU values.

Based on the analysis, the change in emphysema quantity values (LAV%) and values of lung volumes (ml) from the use of FBP B70F and SAFIRE I70f reconstructions was caused by the change in attenuation histogram that affect the change in the lung density. Furthermore, the calculation of the value of the quantity of emphysema (LAV%) is quantitatively conducted by using post processing software that has been automatically programmed to process the following formula:

$$LAV\%-950HU = \frac{\text{low attenuation volume}}{\text{total lung volume}} \times 100\%$$

The formula is used to calculate the LAV% when the threshold is -950HU. Therefore, the formula is relevant if the change of the values of the lung volumes is aligned with the one of values of the quantity of emphysema (LAV%). The analysis result of the formula is different from Baumueller et al's (4) research which showed that there was significant change in the values of the

quantity of emphysema but not in the values of lung volumes. Thus, the analysis in this research can confirm the previous studies according to the theory of formula determining the values of the quantity of emphysema (LAV%) obtained from certain thresholds.

CONCLUSION

The research shows a significant difference ($p < 0,05$) on the measurement result of the quantity of emphysema and lung volumes. In other words, the use of SAFIRE reconstruction can affect the measurement result of the quantity of emphysema and lung volumes quantitatively by using a post-processing software when compared to FBP reconstruction.

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