Supplement I

The intrapulmonary shunt formula

The intrapulmonary shunt (Qs/Qt) was calculated with the standard formula:

$$Qs/Qt = (C_{c'}O_2 - C_aO_2)/(C_{c'}O_2 - C_vO_2) \quad [4]$$

Where Qs is the amount of blood flow that does not participate in pulmonary gas exchange; Qt is the total cardiac output, $C_{c'}O_2$ is the alveolar oxygen content, C_aO_2 is the arterial blood oxygen content, and C_vO_2 is the mixed venous blood oxygen content.

The oxygen content of each portion of blood (C_xO_2) can be calculated by:

$$C_xO_2 = 1.34 \times Hb \times S_xO_2 + P_xO_2 \times 0.0031 \quad [5]$$

Where 1.34 is the volume of oxygen carried by fully saturated hemoglobin, Hb is the hemoglobin concentration (g/dL), S_xO_2 is the fraction of hemoglobin saturated with oxygen, P_xO_2 is the partial pressure of oxygen, and 0.0031 is the Bunsen solubility coefficient for oxygen in plasma.

We assumed that $P_{c'}O_2$ equals the alveolar partial pressure of oxygen (P_AO_2), considering complete equilibration of partial pressures of oxygen in the alveolus and in the end of the pulmonary capillary blood. Thus, $P_AO_2$was calculated from the alveolar gas equation:

$$P_AO_2 = F_iO_2 \times (P_B - P_{H2O}) - P_ACO_2/RQ + P_ACO_2 \times F_iO_2 \times (1 - RQ)/RQ \quad [6]$$

Where P_B is the ambient barometric pressure (760 mmHg), P_{H2O} is the saturation vapor pressure at room temperature (47 mmHg), RQ is the respiratory quotient, P_ACO_2 is the partial pressure of CO_2 in the alveolus ($P_ACO_2 \approx PaCO_2$), and F_iO_2 is the fraction of inspired oxygen.

When the patient inhaled 100% oxygen (F_iO_2 =1), $C_{c'}O_2$, C_aO_2, and C_vO_2 can be estimated from the simplified equations:

$$C_{c'}O_2 = 1.34 \times Hb \times S_aO_2 + 0.0031 \times (713 - P_aCO_2) \quad [7]$$

$$C_aO_2 = 1.34 \times Hb \times S_aO_2 + 0.0031 \times P_aO_2 \quad [8]$$

$$C_vO_2 = 1.34 \times Hb \times S_vO_2 + 0.0031 \times P_vO_2 \quad [9]$$

Where Hb, S_aO_2, P_aCO_2, P_aO_2, S_vO_2, P_vO_2 were all obtained from the result of blood gas analysis.

Thus, the intrapulmonary shunt equation is expressed as:

$$Qs/Qt = [1.34 \times Hb \times SaO_2 + 0.0031 \times (713 - PaCO_2) - (1.34 \times Hb \times SaO_2 + 0.0031 \times PaO_2)]/[1.34 \times Hb \times SaO_2 + 0.0031 \times (713 - PaCO_2) - (1.34 \times Hb \times S_vO_2 + 0.0031 \times P_vO_2)] \quad [10]$$

Supplement II

Randomization lists

Summary

(I) Randomization algorithm: random sorting.
(II) Number of groups: 5.
(III) Total sample size: 75.
(IV) Group sample sizes: actual; target.

P_{LIP2}: 15; 15.
P_{LIPS}: 15; 15.
P_{STAT}: 15; 15.
P_{DYN}: 15; 15.
P_0: 15; 15.

(V) References:

(i) Piantadosi S. Clinical Trials: A Methodological Perspective. Hoboken: John Wiley & Sons, 2005.

(ii) Pocock SJ. Clinical Trials: A Practical Approach. Hoboken: John Wiley & Sons, 1983.

(iii) Rosenberger WF, Lachin JM. Randomization in Clinical Trials: Theory and Practice. Hoboken: John Wiley & Sons, 2002.

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Table S1 Randomization lists

Subject ID	Group assignment	Largest % deviation from target	Cumulative sample size [P_{LIP2}, P_{STAT}, P_{LIPS}, P_{DYN}, P_0]
1	P_{LIP2}	5.3%	[1, 0, 0, 0, 0]
2	P_{STAT}	4.0%	[1, 0, 1, 0, 0]
3	P_{LIPS}	4.0%	[1, 1, 1, 0, 0]
4	P_{DYN}	5.3%	[1, 1, 1, 1, 0]
5	P_{LIPS}	6.7%	[1, 2, 1, 1, 0]
6	P_{DYN}	8.0%	[1, 2, 1, 2, 0]
7	P_{LIPS}	10.7%	[1, 3, 1, 2, 0]
8	P_{DYN}	10.7%	[1, 3, 1, 3, 0]
9	P_{LIP2}	12.0%	[2, 3, 1, 3, 0]
10	P_{LIP2}	13.3%	[3, 3, 1, 3, 0]
11	P_{STAT}	14.7%	[3, 3, 2, 3, 0]
12	P_{LIP2}	16.0%	[4, 3, 2, 3, 0]
13	P_0	10.7%	[4, 3, 2, 3, 1]
14	P_{STAT}	12.0%	[4, 3, 3, 3, 1]
15	P_0	6.7%	[4, 3, 3, 3, 2]
16	P_{LIP2}	12.0%	[5, 3, 3, 3, 2]
17	P_{LIPS}	10.7%	[5, 4, 3, 3, 2]
18	P_{LIP2}	16.0%	[6, 4, 3, 3, 2]
19	P_{LIPS}	14.7%	[6, 5, 3, 3, 2]
20	P_{DYN}	13.3%	[6, 5, 3, 4, 2]
21	P_{DYN}	14.7%	[6, 5, 3, 5, 2]
22	P_{LIPS}	16.0%	[6, 6, 3, 5, 2]
23	P_0	10.7%	[6, 6, 3, 5, 3]
24	P_{STAT}	12.0%	[6, 6, 4, 5, 3]
25	P_0	6.7%	[6, 6, 4, 5, 4]
26	P_{DYN}	8.0%	[6, 6, 4, 6, 4]
27	P_{DYN}	10.7%	[6, 6, 4, 7, 4]
28	P_{DYN}	16.0%	[6, 6, 4, 8, 4]
29	P_0	14.7%	[6, 6, 4, 8, 5]
30	P_{LIP2}	13.3%	[7, 6, 4, 8, 5]
31	P_0	14.7%	[7, 6, 4, 8, 6]
32	P_{DYN}	17.3%	[7, 6, 4, 9, 6]
33	P_{LIPS}	17.3%	[7, 7, 4, 9, 6]
34	P_{STAT}	14.7%	[7, 7, 5, 9, 6]
35	P_{LIPS}	13.3%	[7, 8, 5, 9, 6]
36	P_{DYN}	18.7%	[7, 8, 5, 10, 6]
37	P_{DYN}	24.0%	[7, 8, 5, 11, 6]
38	P_{STAT}	22.7%	[7, 8, 6, 11, 6]
39	P_{STAT}	21.3%	[7, 8, 7, 11, 6]
40	P_{LIP2}	20.0%	[8, 8, 7, 11, 6]
41	P_{STAT}	18.7%	[8, 8, 8, 11, 6]
42	P_{LIP2}	17.3%	[9, 8, 8, 11, 6]
43	P_{STAT}	17.3%	[9, 8, 9, 11, 6]
44	P_{LIPS}	18.7%	[9, 9, 9, 11, 6]
45	P_{STAT}	20.0%	[9, 9, 10, 11, 6]
46	P_{STAT}	21.3%	[9, 9, 11, 11, 6]
47	P_0	16.0%	[9, 9, 11, 11, 7]
48	P_{LIPS}	17.3%	[9, 10, 11, 11, 7]
49	P_0	12.0%	[9, 10, 11, 11, 8]
50	P_{LIPS}	13.3%	[9, 11, 11, 11, 8]
51	P_0	8.0%	[9, 11, 11, 11, 9]
52	P_{LIPS}	10.7%	[9, 12, 11, 11, 9]
53	P_0	10.7%	[9, 12, 11, 11, 10]
54	P_{LIPS}	14.7%	[9, 13, 11, 11, 10]
55	P_{DYN}	13.3%	[9, 13, 11, 12, 10]
56	P_{LIP2}	12.0%	[10, 13, 11, 12, 10]
57	P_0	10.7%	[10, 13, 11, 12, 11]
58	P_{LIP2}	9.3%	[11, 13, 11, 12, 11]
59	P_{STAT}	8.0%	[11, 13, 12, 12, 11]
60	P_{DYN}	6.7%	[11, 13, 12, 13, 11]
61	P_{LIP2}	8.0%	[12, 13, 12, 13, 11]
62	P_{LIP2}	9.3%	[13, 13, 12, 13, 11]
63	P_0	4.0%	[13, 13, 12, 13, 12]
64	P_{STAT}	5.3%	[13, 13, 13, 13, 12]
65	P_{LIPS}	6.7%	[13, 14, 13, 13, 12]
66	P_{LIP2}	8.0%	[14, 14, 13, 13, 12]
67	P_{LIP2}	10.7%	[15, 14, 13, 13, 12]
68	P_{STAT}	10.7%	[15, 14, 14, 13, 12]
69	P_{LIPS}	12.0%	[15, 15, 14, 13, 12]
70	P_{DYN}	13.3%	[15, 15, 14, 14, 12]
71	P_0	8.0%	[15, 15, 14, 14, 13]
72	P_{DYN}	9.3%	[15, 15, 14, 15, 13]
73	P_{STAT}	10.7%	[15, 15, 15, 15, 13]
74	P_0	5.3%	[15, 15, 15, 15, 14]
75	P_0	0.0%	[15, 15, 15, 15, 15]