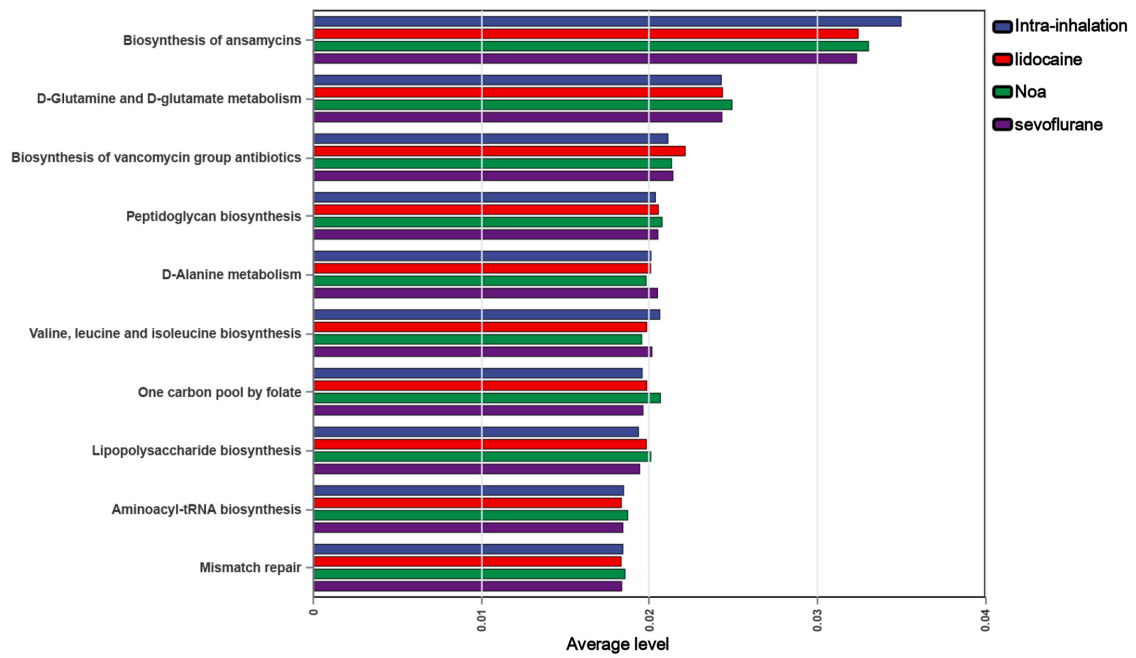


**Figure S1** Linear discriminant analysis effect size (LEfSe) analysis for oral microbiota between the non-anesthesia (Noa) group and the intravenous injection-inhalation (intra-inhalation) group. (A) Linear discriminant analysis (LDA) scores of differential microbes between the Noa and intra-inhalation groups generated by LEfSe analyses. The red and green entries represent differential microbes in the intra-inhalation and Noa groups, respectively. (B) Cladogram depicting the differential microbes between the Noa and intra-inhalation groups from phylum (inside circle) to genus (outside circle).



**Figure S2** Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis reveals metabolic pathways among the four groups. The Y-axis represents the KEGG enrichment pathways, and the X-axis represents the average enrichment levels of samples in different KEGG pathways.

**Table S1** Basic characteristics of participants

Group	Sex	Age (month)	Height (cm)	Weight (kg)
Noa-1	Male	61	112	19.45
Noa-2	Female	26	93	13.5
Noa-3	Female	29	90	14
Noa-4	Male	44	100	20
Noa-5	Female	86	130	26
Noa-6	Female	76	121	23
Noa-7	Female	103	136	31
Noa-8	Male	73	110	15
Noa-9	Male	57	108	20
Noa-10	Female	84	125	23
Noa-11	Male	66	113	20
Noa-12	Male	128	150	52
Noa-13	Female	32	80	14.6
Noa-14	Male	130	160	55
Noa-15	Male	132	161	12.5
lidocaine-1	Male	86	130	45
lidocaine-2	Female	96	126	20.5
lidocaine-3	Male	32	95	17.5
lidocaine-4	Female	96	136	28
lidocaine-5	Female	108	130	24
lidocaine-6	Female	79	120	21
lidocaine-7	Female	77	121	26
lidocaine-8	Female	82	125	25
lidocaine-9	Male	71	115	19.5
lidocaine-10	Female	59	110	20
lidocaine-11	Female	60	113	17.7
lidocaine-12	Male	104	130	25
lidocaine-13	Male	94	127	26
lidocaine-14	Female	59	108	16
lidocaine-15	Male	27	85	12
sevoflurane-1	Female	57	110	17
sevoflurane-2	Female	66	115	21
sevoflurane-3	Male	123	136	33
sevoflurane-4	Female	104	123	25
sevoflurane-5	Male	63	110	18
sevoflurane-6	Female	71	116	20
sevoflurane-7	Male	104	129	24.5
sevoflurane-8	Female	79	125	23
sevoflurane-9	Male	121	149	45
sevoflurane-10	Male	104	142	44
sevoflurane-11	Female	57	112	18
sevoflurane-12	Male	87	123	25
sevoflurane-13	Male	39	97	16
sevoflurane-14	Female	24	80	10.5
sevoflurane-15	Male	80	125	26
intra-inhalation-1	Female	59	110	19
intra-inhalation-2	Female	105	141	26
intra-inhalation-3	Female	90	125	26
intra-inhalation-4	Male	59	115	19
intra-inhalation-5	Male	90	125	26
intra-inhalation-6	Female	76	125	23
intra-inhalation-7	Male	84	129	32
intra-inhalation-8	Male	48	105	15
intra-inhalation-9	Male	95	115	25
intra-inhalation-10	Female	40	100	17
intra-inhalation-11	Male	67	115	21
intra-inhalation-12	Male	59	115	18.5
intra-inhalation-13	Female	75	115	23
intra-inhalation-14	Female	75	125	22
intra-inhalation-15	Male	104	140	25

Noa: Non-anesthesia; intra-inhalation: Intravenous injection-inhalation.

**Table S2** Mantel test of individual factors

Environmental factor	Statistic r	Significance P
Sex (1 or 2)	-0.004170121	0.51
Age (month)	-0.011244863	0.59
Height (cm)	0.024105738	0.30
Weight (kg)	-0.026308806	0.65

To facilitate the assessment of the impact of sex on the data in this study, we recorded male subjects as “1” and female subjects as “2”.

**Table S3** F test for demographic characteristics and clinical parameters

Environmental factor	Group				F value	P value
	Noa	Lidocaine	Sevoflurane	Intra-inhalation		
Sex (1 or 2)	1.47±0.52	1.67±0.49	1.47±0.52	1.47±0.52	0.578	0.63
Age (month)	75.13±35.86	75.33±24.30	78.60±28.93	75.07±19.75	0.057	0.98
Height (cm)	119.27±24.70	118.07±14.09	119.47±17.24	120.00±11.56	0.032	>0.99
Weight (kg)	23.94±13.04	22.88±7.54	24.40±9.71	22.5±4.39	0.139	0.94

To facilitate the assessment of the impact of sex on the data in this study, we recorded male subjects as “1” and female subjects as “2”. Data are presented by mean ± SD. Noa: Non-anesthesia; intra-inhalation: Intravenous injection-inhalation.

**Table S4** Differential microbes between the four groups

Taxon	Intra-inhalation_ average	Lidocaine_ average	Noa_ average	Sevoflurane_ average	P value
<i>Prevotella_nanceiensis</i>	0.010296469	0.027020038	0.032141703	0.025699546	0.04
<i>Campylobacter_showae</i>	0.005044614	0.001547216	0.000787335	0.00105657	0.04

Noa: Non-anesthesia; intra-inhalation: Intravenous injection-inhalation.

**Table S5** Differential microbes between the intra-inhalation and sevoflurane groups

Taxon	Intra-inhalation_average	Sevoflurane_average	P value
Neisseria	0.140964021	0.180696557	>0.99
(Unassigned)	0.113138049	0.13671117	>0.99
Streptococcus	0.112356914	0.127650172	>0.99
Prevotella_7	0.11890269	0.099372523	>0.99
Veillonella	0.087206465	0.064413595	>0.99
Prevotella	0.043766633	0.048419794	>0.99
Leptotrichia	0.058535592	0.032457877	>0.99
Fusobacterium	0.049948411	0.039938891	>0.99
Alloprevotella	0.030326137	0.05493723	0.26
Porphyromonas	0.02696867	0.049766855	0.36
Haemophilus	0.018117569	0.016596037	0.86
Gemella	0.01317746	0.01678645	>0.99
Actinomyces	0.015506698	0.014172036	>0.99
Rothia	0.013361674	0.015659914	>0.99
Lautropia	0.014694564	0.012494631	>0.99
Aggregatibacter	0.010021034	0.012223624	0.86
Capnocytophaga	0.012795749	0.008915753	>0.99
Campylobacter	0.014983284	0.005916971	>0.99
Prevotella_6	0.012600908	0.007109045	>0.99
Granulicatella	0.009530389	0.007719252	>0.99
Prevotella_2	0.008043396	0.002227388	>0.99
Moraxella	0.001765969	0.008501273	>0.99
Megasphaera	0.006542234	0.003564707	>0.99
Selenomonas_3	0.008477361	0.001276209	>0.99
Corynebacterium	0.007983173	0.001732315	>0.99
Bergeyella	0.001701317	0.00443175	0.86
Treponema_2	0.003856969	0.001885531	>0.99
Streptobacillus	0.002385918	0.002718034	>0.99
Abiotrophia	0.001942212	0.002183992	>0.99
Stomatobaculum	0.002817226	0.00109731	>0.99
Lachnoanaerobaculum	0.002431972	0.001332891	>0.99
Oribacterium	0.001848334	0.001766855	>0.99
Cardiobacterium	0.002280527	0.000980405	>0.99
uncultured	0.001795195	0.001324034	>0.99
Vibrio	0.002841138	0.000209897	>0.99
Enterococcus	0.002829625	0.000128418	>0.99
Ruminococcaceae_UCG-014	0.001454223	0.000829846	>0.99
Tannerella	0.001352375	0.000710285	>0.99
Kingella	0.001184103	0.000704085	>0.99
Lactobacillus	0.001334662	0.000530499	>0.99
Bifidobacterium	0.001762427	3.19E-05	>0.99
Johnsonella	0.00137983	0.000356914	>0.99
Dialister	0.001336433	0.000363113	>0.99
Selenomonas	0.001381601	0.000239123	>0.99
Ralstonia	0.000551755	0.000626149	>0.99
Comamonas	0.0008697	0.000279863	>0.99
Acinetobacter	0.00067663	0.000446363	>0.99
Burkholderia-Caballeronia-Paraburkholderia	0.000124875	0.000990147	>0.99
Pseudoalteromonas	0.000919296	0.000102734	>0.99
Atopobium	0.000460534	0.00045522	>0.99
Catonella	0.000560611	0.000323259	>0.99
Simonsiella	0.000128418	0.000727112	>0.99
F0058	0.00068283	0.000154987	>0.99
Peptostreptococcus	0.000588952	0.000226724	>0.99
F0332	0.000278091	0.000450792	>0.99
Solobacterium	0.000307318	0.000388797	>0.99
Prevotella_1	9.30E-05	0.000597808	>0.99
Serratia	0.000583638	3.90E-05	>0.99
Anaeroglobus	0.000497731	4.34E-05	>0.99
Butyrivibrio_2	0.000381712	0.000151445	>0.99
Achromobacter	6.82E-05	0.000458762	>0.99
Filifactor	0.000427765	6.64E-05	>0.99
Mogibacterium	0.000225839	0.000185099	>0.99
Lactococcus	0.000265692	1.77E-05	>0.99
Bradyrhizobium	0.000153216	0.000119562	>0.99
Sphingomonas	0.000178014	4.25E-05	>0.99
Stenotrophomonas	0.000100077	0.000110705	>0.99
Peptococcus	0.000115133	8.94E-05	>0.99

intra-inhalation: Intravenous injection-inhalation.